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EDITORIAL

On the front cover of this Journal will be seen a line drawing of John Snow. This is fitting in view of the fact that this issue contains the first instalment of "On the Inhalation of the Vapour of Ether" which, as we announced last quarter, we are intending to reproduce in serial form.

Our readers may be interested to hear that it is proposed to decorate the hitherto rather uninteresting cover of the Journal with similar line drawings of the three other great British pioneers in anæsthesia—one to each quarter.

Readers of our Journal will remember that Mr. Justice Oliver declared that a recently qualified House Surgeon should not be allowed to have access to a barbiturate for the purpose of anæsthetizing a patient. The General Medical Council through its duly appointed examiners had declared some months previously that she was so qualified. This house divided against itself—this contradiction between two branches of the law, for the General Medical Council is constituted by law, cannot be allowed to persist. Apart from the absurdity of the position it is doing con-

siderable harm. Many recently qualified housemen are unwilling to give anæsthetics and not unnaturally so after Mr. Justice Oliver's statement. While they are in hospital is the best possible time for the recently qualified to give anæsthetics, for they are then nearly always in the presence of some senior member of the staff, who can give them advice and assistance. Missing this experience they go out into the world to practise on their patients, less competent and less well fitted for the tasks that fall to their lot than they would have been had they taken advantage of their opportunities while in hospital. It is time this state of affairs was ended.

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TACHYPNŒA DURING THE ADMINISTRATION OF TRICHLORETHYLENE

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IT is generally agreed that a rise in respiratory rate occurs more frequently during the use of trichlorethylene (Trilene) than with any of the other volatile agents in common use in anæsthesia. In this investigation the incidence, predisposing factors, theories of causation, dangers, prophylaxis, and treatment of this troublesome complication have been studied. The investigation is limited to the use of N_2O-O_2-Trilene in anæsthesia, and no cases of analgesia with the drug are included in this series. All subjects received Trilene from the chloroform bottle of a standard Boyle's apparatus. Tachypnœa has been classed as "mild" with respiratory rates of 28–35 per minute, and "severe" with rates of over 35 per minute. For a rise in respiratory rate to be considered a tachypnœa in this study it must have persisted for at least five minutes.

INCIDENCE OF TACHYPNOEA

The maximum respiratory rates observed during 437 administrations of Trilene are shown in table I. In this series about one-third of all classes developed a definite and persistent tachypnœa. These figures are compared with those of Ayre (1944), who recorded this complication in about half of the 105 cases he reported. The significance of the different incidence of increased respiratory rate in the two series will be discussed later.

TABLE I

Maximum respiratory rates recorded during 437 administrations of Trilene. The observations of Ayre (1944) are included for comparison.

Respiratory rate per minute	No. of cases	Percentage	Findings of Ayre (1944)
20 and under	108	25	13%
21–30	176	40	44%
31–40	105	24	33%
41–50	37	8	6%
51 and over	11	3	4%

PREDISPOSING FACTORS

Of the predisposing factors of tachypnœa with Trilene, youth seems to be the most important, as can be seen from table II and figure 1. These show relationship of age to

TABLE II

Showing relationship of tachypnœa during Trilene anæsthesia to age of patient. Only percentages of total cases in each age group are shown.

	Respiratory rates			
Age in years	Under 28/min.	28–35/min.	Over 35/min.	No. of cases
Under 10	12%	33%	55%	30
11–20	64%	17%	19%	42
21–30	75%	12%	13%	67
31–40	84%	10%	6%	78
41–50	66%	20%	14%	68
51–60	61%	23%	16%	55
61–70	52%	28%	20%	42
71 and over	45%	33%	22%	18
				400

maximum respiratory rate in 400 subjects anæsthetized with nitrous oxide-oxygen-Trilene. Respiratory rates of over 28 per minute occurred in 88 per cent of subjects aged 10 years and under, while the figure for those between 31 and 40 years was only 16 per cent. Tachypnœa was also slightly more common in elderly subjects. This association of youth and a tendency to increased respiratory rates is

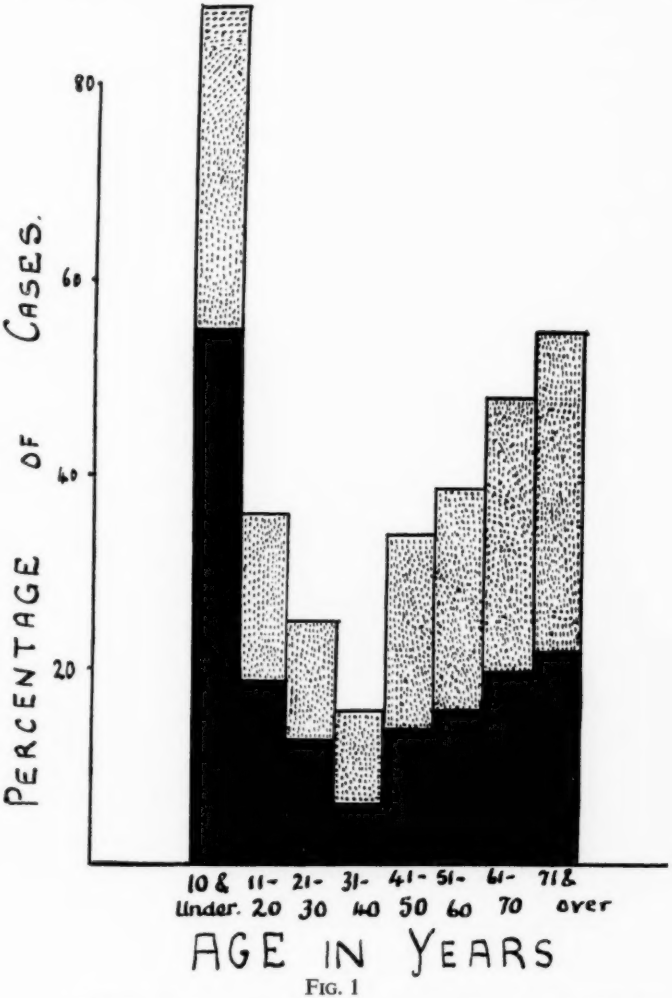

FIG. 1

Histogram showing relationship of maximum respiratory rate during the administration of Trilene to the age of the patient in 400 subjects.

Black = severe tachypnœa (over 35/min.)
Stippled = mild tachypnœa (28–35/min.)

in agreement with the observations of Brittain (1948). In his series of 250 administrations of Trilene for neurosurgery, the only cases of persistent tachypnœa which would not respond to any treatment occurred in children.

The method of induction of anæsthesia as an ætiological factor was studied in 413 patients, the results being shown in table III and figure 2. The highest incidence of

TABLE III

Showing relationship of the incidence of tachypnœa during Trilene anæsthesia to the induction dose of thiopentone. Figures are expressed as percentage of total in each group.

Induction dose of thiopentone	Respiratory rates			No. of cases
	Under 28/min.	28–35/min.	Over 35/min.	
Nil (N_2O-O_2)	13%	38%	49%	38
Under 300 mg.	33%	30%	37%	46
300–500 mg.	58%	25%	17%	139
Over 500 mg.	80%	16%	4%	190
				413

tachypnœa occurred when anæsthesia was induced with nitrous oxide-oxygen. Of those who received thiopentone, the greater the induction dose of barbiturate the smaller became the increase in respiratory rate. This finding is related to the previous one concerning age and incidence of tachypnœa. Very young patients form the majority of subjects induced with nitrous oxide-oxygen and a large proportion of those receiving less than 300 mg. thiopentone belonged to the extremes of age. However, irrespective of age, there is a relationship between the method of induction and incidence of tachypnœa with Trilene, as it was soon found that a fairly reliable method of producing a rise in respiratory rate (for experimental purposes) was to induce anæsthesia with nitrous oxide-oxygen or an amount of thiopentone not exceeding 300 mg.

FIG. 2

Histogram showing relationship of tachypnœa during Trilene anæsthesia to the induction dose of thiopentone in 413 subjects.
Black = severe tachypnœa
Stippled = mild tachypnœa

RELATIONSHIP OF TACHYPNOEA TO DOSAGE OF TRILENE

Hewer (1946) considers that tachypnœa should always be regarded as evidence of overdosage with Trilene, of which Enderby (1944) considers it to be the earliest sign. Other writers are not so dogmatic, but all are agreed that it is a common sequela of "pushing" Trilene (Culbert, 1943; Macintosh and Bannister, 1947; Brittain, 1948).

The lower incidence of increased respiratory rates recorded in the present series (table I) as compared with the figures of Ayre (1944) could be partly explained by the different dosage of Trilene employed. In the personal series about half of the cases were undergoing neurosurgical operations, and as far as possible the dosage was limited to 1 drachm (3.5 ml.) per hour, as recommended by Ostlere (1948). Ayre, on the other hand, averaged 2–4 drachms (7–14 ml.) per hour.

In two further series of reported cases the same explanation is tenable. Gordon and Shackleton (1943) found that 78 per cent of cases have respiratory rates ranging between 26 and 46 per minute, and 6 per cent showed rates of over 60 per minute. They used on an average 1.5 drachm (5.5 ml.) of Trilene per hour in a closed circuit, which represents a much higher dosage than with a semi-closed technique. One drachm (3.5 ml.) per 5 minutes for short operations, and one ounce (28 ml.) per hour for long operations were the amounts employed by Haworth and Duff (1943). Respiratory rates of over 40 per minute occurred in 80 per cent of their cases.

A relationship between the incidence of tachypnœa and dosage of Trilene could possibly be deduced from table III. The larger the induction dose of thiopentone, the smaller would be the amount of Trilene required to maintain anæsthesia; hence the lower incidence of tachypnœa with

large induction doses of thiopentone. A similar relationship may hold for table II. The smallest dose of Trilene delivered from the chloroform bottle of the standard Boyle's apparatus may be an overdosage for a child, and to a lesser extent for aged subjects.

It is not true, however, to say that "pushing" Trilene will result in tachypnœa in all patients. In the experiments to which reference is made later it was desired to have respiratory rates of 40 and over per minute. To obtain this, anæsthesia was induced with either nitrous oxide-oxygen or small doses of thiopentone, and nitrous oxide-oxygen was often bubbled through Trilene for periods up to 10 minutes. The resulting respiratory rates recorded in 66 such cases are shown in table IV. Comparing tables

TABLE IV

Maximum respiratory rates recorded in 66 cases to whom very large amounts of Trilene were administered.

Maximum respiratory rates	No. of cases
20 and under	0
21–30	9 (14%)
31–40	24 (35%)
41–50	17 (26%)
51 and over	16 (25%)

I and IV leaves no doubt that the larger the amount of Trilene administered to the patient, the greater is the likelihood of an increase in respiratory rate. Reverting to the original classification, 4 of the 66 cases (6 per cent) showed no tachypnœa and 11 (17 per cent) responded with only a mild tachypnœa (28–35 per min.). Two cases of respiratory arrest occurred; the rates were under 35 per minute in both subjects at the time when respiration ceased.

Two types of cases encountered during this study do not

come under any of the above predisposing causes. In the first type very little Trilene had been given and anæsthesia was too light when the operation commenced. There was an immediate rise in respiratory rate in response to the towel clips or skin incisions. The resulting tachypnœa persisted throughout the operation, even though anæsthesia was ultimately deepened. The only effect of giving more Trilene was to convert rapid deep respiration to rapid shallow respiration. The second type of subject appeared to have a true sensitivity to Trilene. Tachypnœa developed immediately Trilene administration was started, irrespective of dosage. As long as the smallest trace of the agent remained in the anæsthetic mixture the rapid respiration persisted. Three such patients were encountered, all of the 21–40 age group, and on each occasion it was necessary to abandon the use of Trilene.

If an overdose of a drug is considered to be that amount which produces toxic reactions, and if tachypnœa is regarded as a toxic manifestation of Trilene, it is quite true to say that in all subjects tachypnœa is evidence of an overdose of Trilene. A few subjects appear to be hypersensitive and the smallest amount of Trilene is an overdose to them. On the whole, however, in adults it has been found that tachypnœa occurs only when Trilene is "pushed". The converse does not hold true and all subjects do not react to an overdosage of Trilene by an increase in respiratory rate.

THEORIES OF CAUSATION OF TACHYPNOEA

The earliest reported theory is that of Culbert (1943). He postulated that when the amount of Trilene in the blood reached a certain level a histotoxic anoxia resulted, which manifested itself in the rapid shallow breathing of oxygen lack. He based his view on the fact that increasing the

oxygen in the anæsthetic mixture reduced the respiratory rate, and advised that pure oxygen should be administered to all subjects receiving Trilene. This beneficial effect of increasing the percentage of oxygen in the anæsthetic mixture has not been found to be reliable, and in the few cases in whom it resulted in a decrease in the respiratory rate, the fall was only 4–6 respirations per minute and was not maintained. Moreover, Gordon and Shackleton (1943) recorded a very high incidence of tachypnœa when Trilene was administered with pure oxygen. Once tachypnœa is established anoxia may play a part in maintaining it, but it cannot be said that histotoxic anoxia is the sole cause of the increase in respiratory rate that accompanies the administration of Trilene.

Whitteridge and Bülbring (1944, 1946) have studied changes in the activity of pulmonary receptors during anæsthesia and their influence on respiratory behaviour. Two sets of afferent fibres are concerned in the Hering-Breuer reflex control of respiration, viz. stretch receptors which are stimulated by expansion of the alveoli and cut short inspiration, and separate receptors which are stimulated by deflation and initiate inspiration. All volatile anæsthetics increase the excitability of the pulmonary stretch receptors and this increased excitability is largely responsible for the reduction in depth of respiration. The deflation reflexes which produce acceleration of breathing are briefly stimulated and then paralysed by ether, whereas they are stimulated throughout the exposure by Trilene. Whitteridge and Bülbring concluded that the increased respiratory rate during the administration of Trilene is probably due to a characteristic action of this drug which cuts short both inspiration and expiration.

This theory is criticized by Johnstone (1951), who believes that a persistent degree of bronchoconstriction may

follow the inhalation of Trilene, leading to retention of carbon dioxide with consequent increase in the respiratory rate. Evidence in support of this view is supplied by the effect of pethidine in abolishing the tachypnœa. He suggests that pethidine reduces the respiratory rate by dilating the bronchi and bronchioles, thus facilitating the elimination of carbon dioxide. He ignores the depressant effect of pethidine on respiration, especially when given intravenously (Mushin, 1951; Pearce, 1951), as a possible cause of the decrease in respiratory rate. Another action of pethidine is its ability to inhibit laryngeal and pharyngeal reflexes (Ruben and Andreassen, 1951) which are of vagal origin. Cutting the vagus causes respiration to become slow and deep (as after pethidine), presumably because both the stretch receptors and deflation reflexes are abolished. It is probable that at least a part of the action of pethidine in reducing the tachypnœa due to Trilene is due to its depressant action on the Hering-Breuer reflex, to the increased activity of which Whitteridge and Bülbring attributed the increase in respiratory rate.

In an attempt to elucidate this problem, the effects of various drugs of known action were tried on subjects with an established tachypnœa. With two exceptions (amyl nitrite and ether), the drugs were given intravenously and the concentration of Trilene being administered to the patient was not changed until the observations were completed. To make a fair comparison of the various drugs, none was administered to subjects with a respiratory rate of under 40 per minute. Table V summarizes the results obtained with the various drugs.

The findings with pethidine confirm those of Johnstone (1951). His theory is not substantiated by the effects of the other bronchial dilating drugs. Aminophylline (theophylline ethylene diamine) is the most potent of these (Hawkins

TABLE V

Showing effect of various drugs in reducing the respiratory rate during the administration of Trilene.

Drug	Dose	No. of cases		Duration		Average reduction in respiratory rate
		Total	Resp. rate reduced	Max. effect (min.)	of effect (min.)	
Pethidine	25 mg.	16	16 (100%)	5	25	23 per min.
	20 mg.	30	30 (100%)	7	31	12 „ „
Morphine	⅛–¼ gr. (8–10 mg.)	6	6 (100%)	5	90	28 „ „
Procaine HCl	100–200 mg.	32	20 (62%)	2½	6	8 „ „
„ amide	100–200 mg.	10	7 (70%)	7	25	6 „ „
Aminophylline	250 mg.	6	0 (0%)	—	—	—
Aleudrin	0.01–0.5 mg.	10	2 (20%)	2	14	6 „ „
Amyl nitrite	3–5 minims	12	8 (66%)	3	5	10 „ „
Ether		6	4 (66%)	3	9	12 „ „
Antistin	100 mg.	6	0 (0%)	—	—	—

and Schild, 1951), but observations of its action are valueless because of its respiratory stimulant effect (Sperling, Weisman, and Papermaster, 1942). Isopropyl noradrenaline, which has about ten times the bronchial dilating action of adrenaline, was only effective in reducing the respiratory rate in 20 per cent of cases. Doses greater than 0.5 mg. produced a transient tachycardia and rise in blood-pressure. In a few cases, not recorded in table V, in whom this rise in blood-pressure occurred, there was a fall in respiratory rate coincident with, and of similar duration to, the pressure changes. Amyl nitrite and the addition of a high concentration of ether vapour would seem from table V to be fairly effective but, in actual fact, the respiratory rate was only reduced by them in subjects who coughed or held their breath in response to the irritant vapours.

In view of the anti-histamine action of pethidine (Yonkman, 1948) it was considered advisable to try the effect of

Antistin, which, although not a true bronchial dilator, has been used to counteract the bronchospasm produced by curare (Foregger, 1950). Its failure to reduce the respiratory rate on any of the 6 occasions it was used makes it unlikely that the anti-histamine action of pethidine plays any part in its effect on Trilene tachypnœa.

Morphine, which has a similar though less depressant action than pethidine on the respiratory centre, is equally effective in reducing the respiratory rate during Trilene anæsthesia. Its action on the bronchial tree is one of constriction rather than dilatation. The reduction of tachypnœa by morphine and pethidine varies in degree and duration with the respiratory depressant effects of the doses of the two drugs injected, and it is reasonable to assume that their central action on the respiratory centre is the common factor.

The remaining drugs, procaine hydrochloride and procaine amide, abolished the tachypnœa in about two-thirds of the cases in whom they were used. The amide, which is longer acting than the hydrochloride, has a more prolonged effect in reducing the respiratory rate. They are too unreliable to be of use clinically; even in cases of severe tachypnœa the reduction in respiratory rate which they caused was much less than with either morphine or pethidine. The findings with the procaine drugs are of no help in elucidating the cause of the rise in respiratory rate during Trilene anæsthesia as they have a slight bronchial dilating action and slight depressant effect on respiration, as well as being local analgesics which could paralyse the pulmonary receptors in the lungs.

The findings reported above are all in agreement with the view that the occurrence of tachypnœa during the administration of Trilene is due to stimulation by the drug of the pulmonary stretch and deflation receptors. Bronchial

dilating drugs are ineffective in reducing the respiratory rate, and it is highly improbable that bronchial constriction and retention of carbon dioxide is a causative factor.

DANGERS OF TRILENE TACHYPNOEA

One usually considers the main hazard of Trilene to be its effect on the cardiovascular system. Increases in respiratory rate are generally thought to be an annoying, but comparatively harmless, complication of the administration of Trilene. Gordon and Shackleton (1943), Hewer (1946) and Brittain (1948), however, have all drawn attention to the possibility of the shallow rapid respiration causing anoxia. There are no recorded observations as to the extent of this anoxia and its relationship to the respiratory rate.

Quantitative studies of respiratory volumes and arterial blood oxygen content were performed on 8 patients undergoing operation of ligation of bilateral varicose veins. Respiration rates during the administration of Trilene ranged from 14–54 per minute. All subjects received the same flow of gases throughout the investigation, viz. 6 litres of nitrous oxide and 2 litres of oxygen per minute. Minute respiratory volume was recorded by a Glover spirometer and blood oxygen content estimated by the colorimetric method of Exton, Schattner, Korman, and Rose (1945).

Figure 3 shows the changes recorded in minute and tidal volumes at various respiratory rates. For the sake of simplicity, values are expressed as a percentage of those at the respiratory rate of 20 per minute. The consistent rise in minute volume and fall in average tidal volume are what one would expect during tachypnœa with Trilene.

The fall in arterial blood oxygen content associated with these respiratory disturbances is shown in figure 4. As the respiratory rate is doubled from 20–40 per minute, on an

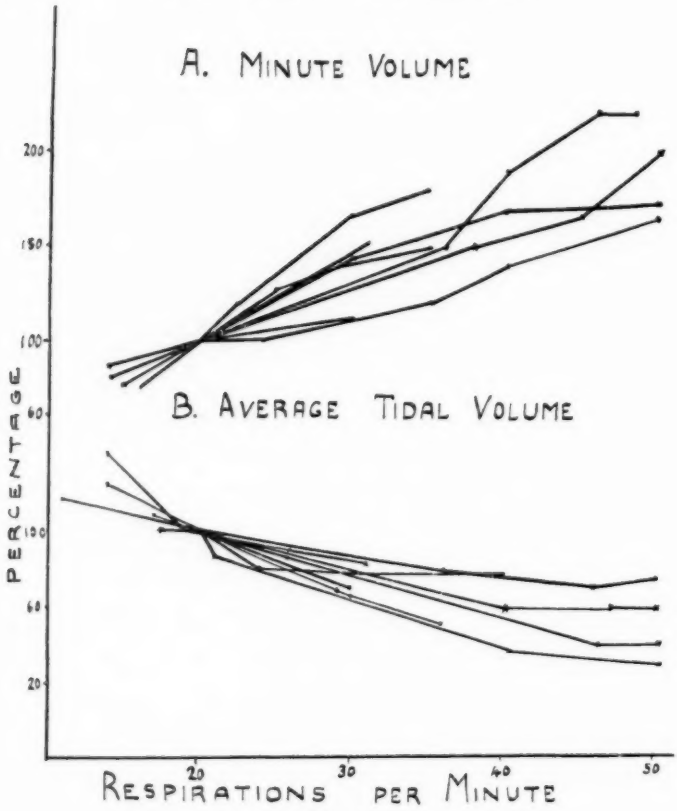

FIG. 3

Changes in minute and average tidal volumes recorded in 8 cases who showed rise in respiratory rate during the administration of Trilene. Values are expressed as a percentage of those for a respiratory rate of 20 per minute.

average the oxygen content of arterial blood fell 25 per cent, and trebling the respiratory rate reduced it by one-third. From these figures it is clear that in the average patient cyanosis would not occur with respiratory rates of under 60 per minute. This is in agreement with the findings

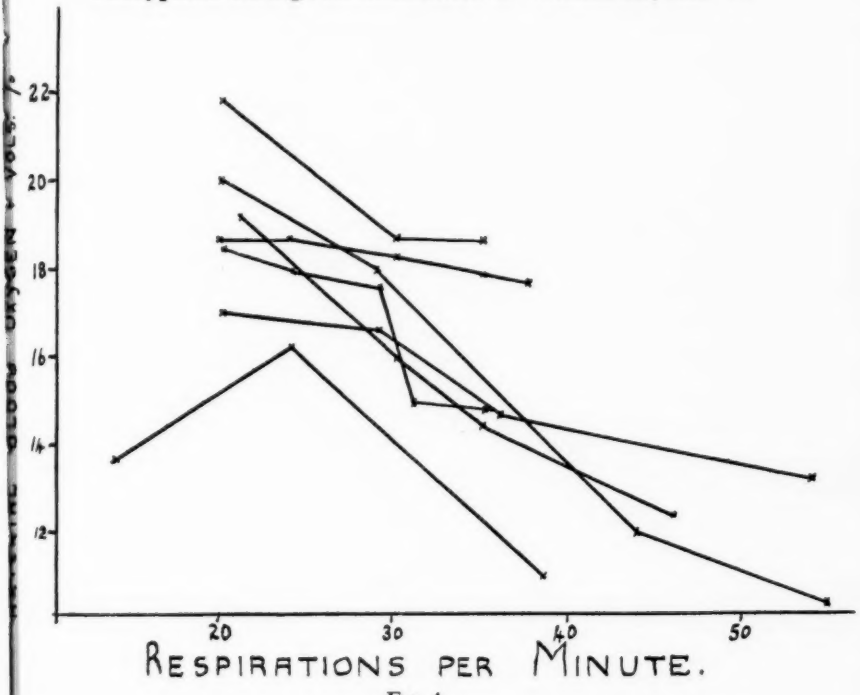

FIG. 4

Arterial blood oxygen content at various respiratory rates in 7 subjects who developed tachypnœa during the administration of Trilene.

of Gordon and Shackleton (1943), who only observed cyanosis with extreme increases in respiratory rate.

In anæmic subjects the fall in oxygen saturation of the blood which occurs with moderate increases in respiratory rate could well be dangerous. The absence of cyanosis gives a false sense of security even in normal patients, and to allow a respiratory rate of 40 or over per minute to persist for long periods during Trilene anæsthesia is quite clearly undesirable. This is of prime importance when Trilene is used in anæsthesia for neurosurgery. The

slightest degree of anoxia manifests itself by a rise in intracranial pressure and increased venous oozing which is so detrimental to such operations (Hunter, 1952).

PROPHYLAXIS AND TREATMENT

In a very small number of adult subjects (less than one per cent) the administration of minute amounts of Trilene results in an increase in respiratory rate. If tachypnœa occurs immediately the drug is introduced into the anæsthetic mixture, it is wise to consider the patient to be sensitive to Trilene and abandon its use. In the majority of cases the onset of tachypnœa can be prevented by using minimal amounts of Trilene (1 dr. (3.5 ml.) per hour). This can best be achieved in adults by the use of an adequate induction dose of an ultra-short acting barbiturate. It may be necessary to give a small supplementary dose of barbiturate five minutes after induction, as by this time diffusion to non-nervous tissues will have taken place and the blood concentration be low. Using the chloroform bottle of the Boyle's apparatus it is often impossible to keep the dosage low enough if the drug is administered continuously. Intermittent administration has proved successful as the low volatility of Trilene and its subsequent low rate of excretion permit satisfactory anæsthesia to be continued by nitrous oxide-oxygen for long periods after Trilene has been cut off. In children this is particularly desirable, for most vapourizing bottles deliver a concentration of Trilene which is an overdose to a child. Theoretically at least, basal narcosis with rectal thiopentone or hexobarbitone should reduce the incidence of tachypnœa in children. Personal experience of this is too small to allow any conclusions to be drawn.

Once tachypnœa is established, the respiratory rate will generally fall if the concentration of Trilene vapour is

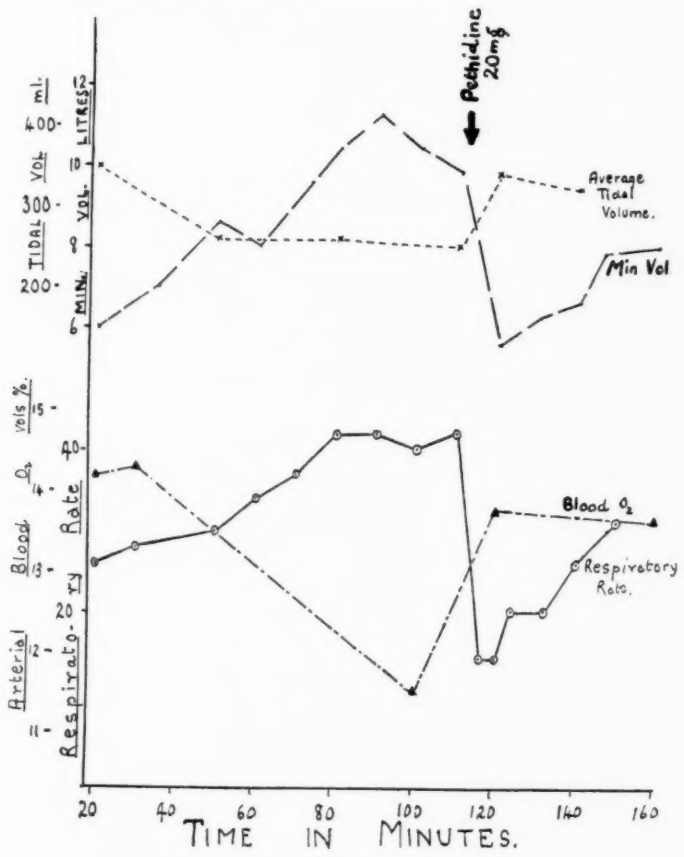

FIG. 5

Showing effect of 20 mg. of pethidine on respiratory rate, minute and tidal volumes and blood oxygen content in a subject who developed tachypnœa during the administration of Trilene.

reduced. It takes some time for this to happen and it may be desirable to reduce the respiratory rate more rapidly because of sub-oxygenation of the patient. Of the drugs shown in table V, pethidine is the most effective, the safest,

and the one most likely to be available without delay. Tachypnœa will be reduced in 2 minutes by 50 mg. pethidine but this dose is frequently followed by apnœa (Johnstone, 1951). To find the safest dose of pethidine, respiratory volumes and arterial blood oxygen content were measured in a series of patients with tachypnœa, before and after doses of pethidine varying from 10–40 mg. The respiratory depression following doses greater than 25 mg. caused a greater decrease in blood oxygen than resulted from the tachypnœa. The most satisfactory results were obtained with 20 mg. pethidine (fig. 5). On an average the effect of this amount reaches its maximum in 5–7 minutes and lasts for 30–35 minutes. Once the pethidine has exercised its full effect there is no necessity to administer Trilene for at least 20 minutes. The dose of pethidine can safely be repeated should a further rise in respiratory rate occur, but should this be necessary it may be as well to continue with nitrous oxide-oxygen-pethidine and abandon the use of Trilene.

As mentioned previously the effect of the procaine drugs is too unreliable for them to be of any clinical value in this respect. Procaine hydrochloride is not entirely free from danger as the following case will show:

A male subject, aged 16, was for exploratory craniotomy for suspected cerebral tumour. Anæsthesia was induced with 500 mg. thiopentone and topical application of Xylocaine to pharynx and larynx using the technique recommended by Hunter (1951). Anæsthesia was continued with endotracheal nitrous oxide-oxygen-Trilene. The respiratory rate was 36 per minute, 65 minutes after induction. Fifty mg. procaine reduced the rate to 32 in 2 minutes when a further 50 mg. were given. Within one minute the respiratory rate was 48 per minute, breathing was stertorous and movements of the head under the towels indicated that the patient was having a convulsion. This was immediately controlled by 50 mg. thiopentone which, incidentally, reduced the respiratory rate to 24 per minute.

This patient had suffered from epileptiform convulsions for the past few months due to the cerebral tumour. His threshold for convulsions was presumably low and 100 mg. procaine given intravenously over a period of 2 minutes was sufficient to initiate a major fit. At the beginning of the operation 40 ml. of 1 per cent procaine (400 mg.) with 1: 200,000 adrenaline was injected into the scalp without any untoward effects. The absorption of this solution would be reduced by the adrenaline and the blood level never reached a sufficiently high level to cause a convulsion. Furthermore, it was given soon after the thiopentone, which would raise the threshold to convulsions.

CONCLUSIONS

1. Tachypnœa occurs in about one-third of all subjects to whom Trilene is administered.

2. It is more common in children and the aged.

3. The larger the dose of thiopentone used to induce anæsthesia the less is the likelihood of an increase in respiratory rate with Trilene.

4. Tachypnœa should be regarded as a sign of overdosage with Trilene.

5. Failure of bronchodilator drugs to abolish tachypnœa is at variance with the view that the increase in respiratory rate is due to bronchoconstriction and retention of carbon dioxide.

6. Findings reported are in agreement with the theory that tachypnœa is due to increased sensitization of the pulmonary stretch and deflation reflexes by Trilene.

7. Minute volume is increased, average tidal volume reduced and arterial blood oxygen level reduced with increases in respiratory rate. The fall in blood oxygen may be detrimental to the patient.

8. Tachypnœa can be prevented in the majority of subjects by the use of minimal doses of Trilene.

9. Pethidine, in doses not exceeding 25 mg. for an adult, will abolish tachypnœa for 30–35 minutes.

10. Intravenous procaine is unreliable and even dangerous as a treatment for tachypnœa during the administration of Trilene.

SUMMARY

1. The incidence of rise in respiratory rate following the use of Trilene is reported. Predisposing factors of age of the subject and induction dose of thiopentone have been studied. A relationship has been shown between the dose of Trilene and the occurrence of tachypnœa.

2. Theories of causation of the increase in respiratory rate have been reported and experimental evidence produced to substantiate them.

3. The effect of tachypnœa on respiratory volumes and arterial blood oxygen content has been studied.

4. The prophylaxis and treatment of tachypnœa during the administration of Trilene are discussed.

ACKNOWLEDGEMENTS

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REFERENCES

Ayre, P. (1944). *Brit. J. Anæsth.*, **19**, 17.
Brittain, G. J. C. (1948). *Curr. Res. Anesth.*, **27**, 145.
Culbert, T. D. (1943). *Brit. med. J.*, **1**, 582.
Enderby, G. E. H. (1944). *Brit. med. J.*, **2**, 300.
Exton, W. G., Schattner, F., Korman, S., and Rose, A. R. (1945). *J. Lab. & clin. Med.*, **30**, 84.
Foregger, R. (1950). *J. Amer. med. Ass.*, **142**, 1344.

Gordon, R. A., and Shackleton, R. P. W. (1943). *Brit. med. J.*, **1**, 380.
Hawkins, D. F., and Schild, H. D. (1951). *Brit. J. Pharmacol.*, **6**, 682.
Haworth, J., and Duff, A. (1943). *Brit. med. J.*, **1**, 381.
Hewer, C. L. (1946). *Brit. med. Bull.*, **4**, 108.
Hunter, A. R. (1951). *Anæsthesia*, **6**, 172.
——— (1952). *Proc. R. Soc. Med.*, **45**, 427.
Johnstone, M. (1951). *Brit. med. J.*, **2**, 943.
Macintosh, R. R., and Bannister, F. (1947). *Essentials of General Anæsthesia*, 4th ed., Oxford: Blackwell.
Mushin, W. W. (1951). *Proc. R. Soc. Med.*, **44**, 840.
Ostlere, G. (1948). *Brit. med. J.*, **1**, 195.
Pearce, C. (1951). *Brit. J. Anæsth.*, **23**, 205.
Ruben, H., and Andreassen, A. K. (1951). *Brit. J. Anæsth.*, **23**, 33.
Sperling, L., Weisman, S., and Papermaster, R. (1942). *Surgery*, **2**, 600.
Whitteridge, D., and Bülbring, E. (1944). *J. Pharmacol.*, **81**, 340.
——— ——— (1946). *Brit. med. Bull.*, **4**, 85.
Yonkman, F. F. (1948). *Annals N.Y. Acad. Sci.*, **51**, 59.

Brit. J. Anæsth. (1953), **25**, 24.

THE APPLICATION OF A METHOD FOR THE INVESTIGATION OF CEREBRAL DAMAGE FOLLOWING ANÆSTHESIA USING CONTROLLED HYPOTENSION—A PRELIMINARY COMMUNICATION

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No clinical test of cerebral function has been performed during voluntary induced hypotension, but in the literature it has been stated that clinically no cerebral changes have been observed. Berg in 1949 reported a method of measuring the functional capacity of the normal cerebrum and after cerebral injuries of a traumatic, toxic or infectious nature. He employed for the purpose of his investigation the "flicker fusion method" (Berg, 1949).

If intermittent flashes of light are directed on the eye it appears as though the light is being alternately turned on and off. When the rate of flashes is increased the light appears continuous, but reduced in intensity. Brighter and darker periods can, however, still be perceived. When the rate of flickering is still further increased, the difference disappears completely and a continuous light is seen. The rate of the intermittent flashes per second at which the flickering impression disappears and is experienced as a continuous light is called the "flicker fusion frequency" (fff). As was shown by Berg, this may also be determined by maintaining a constant flash rate (e.g. 40 per sec.) and varying instead the strength of the light.

Pathological conditions of the retina, optic nerve or optical centres always provide clear changes in the flicker

fusion frequency, whereas injuries to other parts of the central nervous system do not usually yield such variations in rate as to be called abnormal. None the less, on account of the extensive connections between the optical pathways, the optical centre and the central nervous system as a whole, Berg considered that the fff-determination suitably modified could be used as a test of the function of the entire central nervous system. If, at the same time as the fff-determination, the central nervous system is by some means depressed, a hitherto latent lowering of the functional capacity of the central nervous system may be revealed. As a depressant Berg used hexobarbitone (Evipan) in a dose of 10 per cent of the usual induction dosage, as calculated by Specht (1933). In normal patients this depressant dose of hexobarbitone induces a clear, though brief, lowering of the flicker fusion values, but if the patient has been exposed to any cerebral injury, traumatic, toxic, infectious or anoxic, a more persistent lowering of fff is obtained in almost 100 per cent of cases.

In his tests Berg used a variable light intensity. This was achieved in part by introducing wedge filters between the light source and the flicker area, and in part by changing the distance of the light from the flicker area. Without filters the light intensity was 7.2 foot candles and the flicker frequency 40 flashes a second. In order to achieve flicker fusion the light intensity was reduced by filters. The density of the filter was expressed in ordinary logarithms. A filter reducing the light intensity to a half possessed therefore a density equal to the logarithm for 2, i.e. about 0.3; similarly a filter reducing the intensity four times, possessed a density equal to the logarithm for 4, etc. The density in the variable filters varied between 0–0.9. In order to enable him to deal with whole numbers, Berg has introduced a unit which he calls a "filter unit" (Fu). The light intensity

stated in "filter units" expresses how many times the standard intensity must be reduced to cause fusion. One Fu corresponds to a distance on the graph scale of 1 cm., and this corresponds in turn to a filter density of 0.06. Five filter units thus correspond to 5 cm. on the scale and reduce the light intensity by one-half. ($5 \times 0.06 = 0.3$; 0.3 is the logarithm of 2, which, as explained above, indicated a reduction in light intensity of one-half.)

METHOD

The test is performed with the patient in a sitting position. First a careful initial value is obtained. After this the hexobarbitone is given, and two minutes later the first determination is made; subsequently, fusion values are determined every other minute. A curve is thus obtained, in which is seen not only how deep is the drop in fusion value but also for what length of time the fusion value remains below normal. This represents the depth and length of the curve (see figs. 1, 2 and 3). The degree of severity of the cerebral injury is directly proportional to the depth and length of the curve, and moreover it is directly proportional to the number of days after the injury during which the test is still positive.

RESULTS

It is, however, impossible to make use of every case if one insists always on absolutely equivalent test conditions from case to case. The patient must be able to sit up. He must not be so affected by the anæsthetic or operation that he is unable to concentrate on the investigation and thus collaborate effectively.

The patients tested by us are therefore relatively few in comparison with the number of cases in which low-pressure anæsthetics have been used. We are, however, only at the beginning of our investigation and have merely wished to draw attention to the preliminary results.

Up to now we have used the negative cases as controls, but will, of course, later investigate an equivalent control series, which has been exposed to anæsthesia but not to intentional hypotension.

Our interest has been especially directed to those cases in which we have induced a bloodless operative field by combining block of the autonomic nervous system with a raised head-end of the operating table, a situation in which a certain degree of cerebral anæmia must be expected.

TABLE I

No. of tests	*Positive*	*Negative*
15	6	9
Head raised	5	6
Head lowered	1	3

Since the investigation was begun 15 patients have been followed up during their post-operative period with daily flicker fusion tests. Of these 15 patients (table I) 6 have shown a positive test signifying cerebral injury. Of the 6 with positive tests 5 had been lying during the operation and anæsthetic with the head-end of the table raised between 10 and 20 degrees. One of the patients with a positive test was operated in the lateral position with the operating table horizontal.

The curves for this latter patient and two of the patients with a raised head-end are shown in figures 1–3.

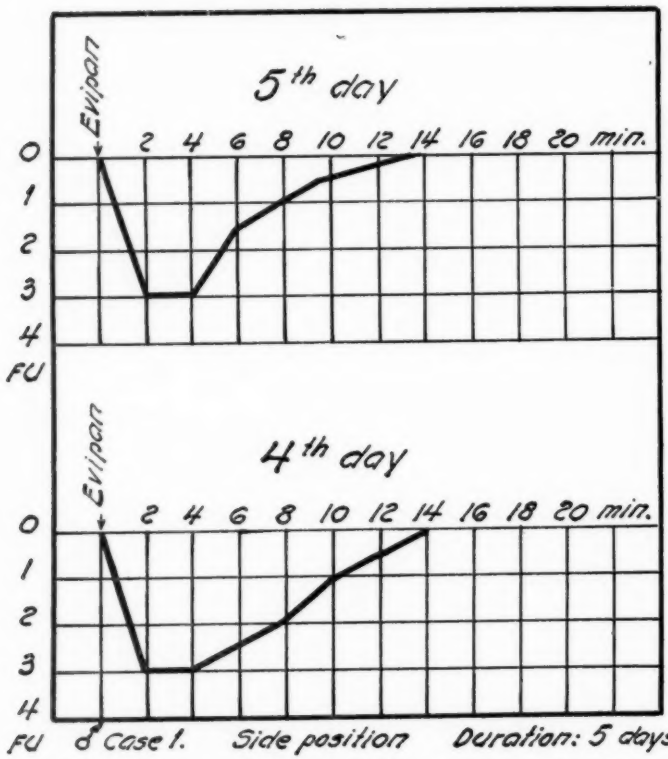

FIG. 1. *Case* 1. Male patient 23 years. Extra-pleural pneumonolysis. Operation in lateral position. Syst. blood pressure < 80 mm. for 2¼ hours. Very slight bleeding. Hexobarbitone test positive for 5 days. Negative test on 6th day. Post-operative course otherwise without complications.

DISCUSSION

The cerebral injuries thus demonstrated are not serious. Their frequent appearance in this scanty material may, of course, be merely accidental, but in our opinion this is scarcely credible. Further investigation, however, must provide the answer. Attention to this point should be of

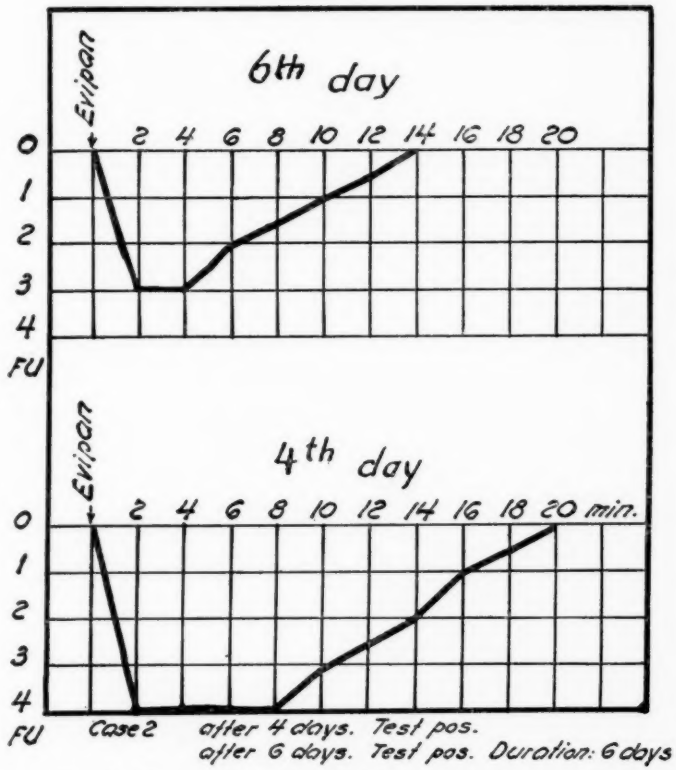

FIG. 2. *Case* 2. Male patient 52 years. Extirpation of malignant melanoma on face. Operation with raised head-end (20°). Syst. blood pressure 40–70 mm. for 1½ hours. Very slight bleeding in operation wound. Hexobarbitone test positive for 6 days. Negative on 7th day. Post-operative course otherwise without complication.

especial importance in those cases where a protracted plastic surgical repair may require repeated hypotensive anæsthetics at short intervals.

The hexamethonium technique, or, perhaps more correctly, the low-pressure technique, is in comparatively fre-

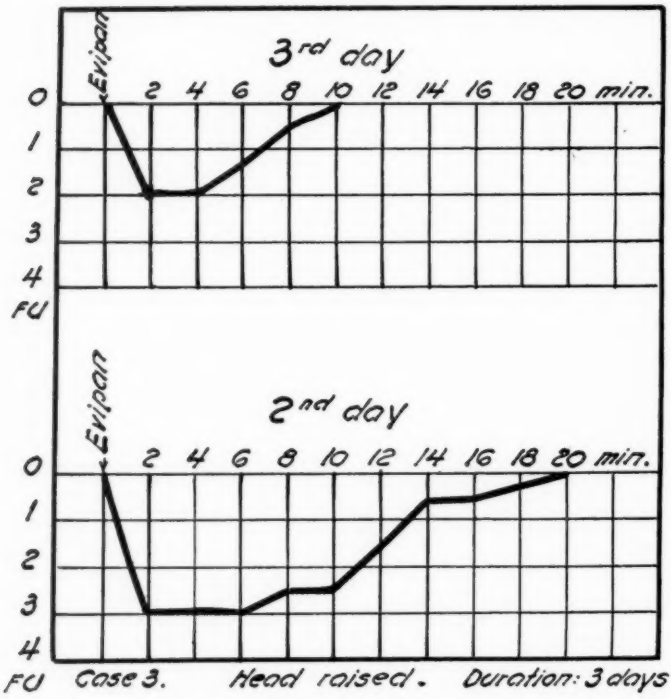

FIG. 3. *Case* 3. Female patient 44 years. Operation for carc. mammae. Operating table with raised head-end (15°). Syst. blood pressure 65–85 for 1 hour. No bleeding in operation area. Hexobarbitone test positive for 3 days. Negative on the 4th day. Post-operational course otherwise without incident.

quent use today: in my personal opinion, too frequent. Its definite place in the anæsthetist's armoury has not yet been determined. A word of warning is, therefore, in place. The technique is not without risk, and accidents, even fatalities, have occurred.

I would like to point out in conclusion that in modern practice it would seem that the indication for this technique is not always to facilitate the surgeon's work. The question

as to whether the technique, which is not altogether free from risk, will afford a better chance for the surgeon to perform an operation of *vital* interest to the patient must, in my opinion, be the only factor which will decide in each individual case whether its use is justified.

SUMMARY

The author has investigated patients, operated upon under controlled hypotension, induced by hexamethonium, postoperatively by the effect of depression with hexobarbitone on the flicker fusion intensity *ad modum* Berg.

Fifteen patients were studied, 6 of whom showed a positive test indicating a cerebral injury, presumably anoxic in origin. Postural ischæmia of the brain seems to be especially dangerous. The injuries were not severe but resembled concussion. Repeated trauma to the brain of this nature might lead to severe and irreversible damage.

It is therefore our opinion that the indications for using the technique with controlled hypotension and postural ischæmia must be very clear and each case carefully evaluated.

The investigation is being continued.

REFERENCES

Berg, O. (1949). *Acta psychiat., Kbh.*, Suppl. 58.

Specht, Karl (1933). Quoted by Adams, R. Charles (1944). *Intravenous Anesthesia,* London: Hoeber.

Brit. J. Anæsth. (1953), **25**, 32.

LARYNGEAL LESIONS FOLLOWING ENDOTRACHEAL ANÆSTHESIA: A REPORT OF TWELVE ADULT CASES

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LARYNGEAL complications of endotracheal anæsthesia are remarkably rare, considering the large number of patients rendered liable to them. Nevertheless, in three years of routine ear, nose and throat practice, we have seen twelve cases. Some have suffered severe disability, whilst others have been symptomless, and of interest only to the observer.

Our cases correspond closely to those reported elsewhere (see additional references), and we believe that a brief clinical description may be of interest to general surgeons and anæsthetists, as well as to laryngologists.

THE LESIONS

The following summary is based on cases which have been recorded in sufficient detail in the literature, and the present series.

Should examination be performed within a few days of the anæsthetic, the appearances are those of an acute laryngitis, but when this general inflammation subsides a small area of ulceration may be seen at the glottis, usually on the vocal process of one or both arytenoid cartilages. Granulations may proliferate at the site of ulceration, and in certain cases they organize to form a polypus or a more or

less pedunculated "fibroma", in the course of time. Apparently a similar nodule may form as a submucosal hæmatoma (Clausen, 1932).

No matter how they may be generated, these masses quite frequently disappear spontaneously, but may need to be removed. In either case there is a tendency to web-formation later. Not infrequently the site of these changes is just below the glottis.

SYMPTOMS

Some of the cases are *symptomless* throughout, while in others, complaints arise long after the operation. Four of those described here were found amongst some three hundred routine laryngoscopies following thyroidectomy. It would seem likely that many lesions pass unrecognized through lack of a special laryngoscopic examination after intubation.

However, *hoarseness* is usually present from the time of operation; but may not be noticed for some weeks, and may vary deceptively.

Intermittent loss of voice usually occurs when a mobile polypus is present.

Continuous dyspnœa may be much worse than the glottic appearance suggests (Case 3). Possibly turbulence of the airstream can prevent a free flow of air through the larynx, and would result from even a slight interference with the shape of its cavity. Possibly there may be web formation lower in the trachea, although we have not directly observed it. In only one, atypical, case was dyspnœa associated with definite fixation of the cords.

Acute dyspnœa is rarely serious, but has been described, and in one of the present series tracheostomy was necessary.

Pain or *discomfort* in the throat, and, rarely, *hæmoptysis*, may occur in the first few weeks; and later there may be *a*

sensation of something moving in the throat if a pedunculated polypus is present.

AETIOLOGY

The possible causes of trauma are legion, and it is not surprising that one cannot deduce, from a relatively small number of case records, when the damage is most likely to have occurred. We have to consider the following:

1. *Injury may occur in passing or removing the tube*, especially when the anæsthetic is too light for the manœuvre. As laryngologists, we ourselves prefer to see a tube passed under vision, but among cases in which details of technique are described, a smaller number has followed the blind nasotracheal than the other methods. The numbers are too few to enable one to arrive at a conclusion.

After an oral or nasal operation, the anæsthetist may not like to disturb his tube and pack until the protective laryngeal cough reflex has returned, and then will be particularly gentle in removing the tube to avoid abrasion of the cords.

2. *Movement between the tube and cords* after the former is in position, (*a*) by coughing, particularly when the effort causes an extension-flexion movement of the neck, and by attempts to extrude the tube and packing, and (*b*) in attaining a special position of the head, as, for example, with the cranial head-rest (Crispell and Hampton, 1950).

3. *Pressure by the tube* is considered important by Dwyer and his colleagues (1949), who demonstrated convincingly that its usual curve may force the tube into the back of the glottis, and at the same time against the front of the trachea. They suggested a double curved tube, which had to be introduced with a stilet. One would expect the

stiffer tubes, favoured in blind nasal intubation, to press more firmly on the interarytenoid region than the softer ones it is possible to introduce with a laryngoscope.

4. We have been unable to show a relation between these injuries and *the material of which the tube is made*, or any particular *antiseptic or lubricant used*, but have in mind the possibility of reaction to certain synthetic tubes, and idiosyncrasy to local anæsthetics, paraffins, etc.

5. The possibility of introducing *infection* to an otherwise insignificant abrasion of the cord is discussed by Crispell and Hampton, who mention that streptococci have been cultured from the lubricants used. Almost invariably the histologist's report on nodules removed at operation states that there is evidence of secondary infection, and perhaps it is inevitable in this region.

The condition we are describing is essentially one of adults, occurring at any mature age. Acute œdema of the larynx, sometimes necessitating tracheostomy, seems to be the corresponding effect in the lax tissues of childhood.

There is no doubt that these lesions are seen very much more frequently in women than men; the twelve cases reported hereafter are all female. New and Devine (1949) observed that contact ulcer granuloma of the larynx, probably identical with the intermediate stages of the condition we are describing, occurs more frequently in men—"except as a result of intubation, when women are chiefly affected."

It is our impression that these lesions are more common now than they were in the earlier days of endotracheal anæsthesia, but our attention has been drawn to the possibility that it was because Kuhn's tube traumatized the larynx in a similar way that many people gave it up.

TREATMENT

With regard to *prevention*, we should like to stress the importance of gentle respiration when the tube is being passed, and immediately afterwards, and indeed until it is finally withdrawn from the larynx. A violent fit of coughing after intubation must be traumatic; and perhaps this is more likely to occur with the rapid induction techniques of to-day, in any but the most experienced hands, than with a slow progress to a deep level of anæsthesia, and an unhurried view of the cords.

In the early stages *complete voice rest* will help the ulcer to heal rapidly, without the formation of excessive granulation tissue.

There is a tendency for the nodule to disappear naturally, and *removal* should be postponed until it is apparent that this is not going to take place. But eventually symptoms may dictate the necessity for excision—and this is usually easy enough, simple snaring or punching-out of the lesion by direct laryngoscopy being sufficient. However, the operation may have to be repeated, and this too should not be done before some time has elapsed.

THE CASES

Case 1. Female, aged 45. May 1948. Pan-hysterectomy.

12th week. "Voice husky since operation, and occasionally it goes to a whisper." Fibrous-looking nodule attached to the under surface of the right cord, inflammation about its base (fig. 1); removed at direct laryngoscopy. Microscopy: "Tissue containing numerous fibroblasts, dilated blood vessels and lymph spaces and old hæmorrhage, infiltrated with chronic inflammatory cells; suggestive of traumatic origin, with subsequent infection."

28th week. Larynx normal.

22nd month. Larynx normal.

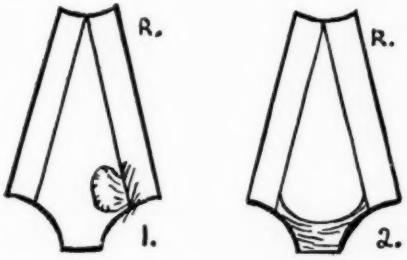
Case 2. Female, aged 24. 30th March, 1949. A difficult appendicectomy.

12th day. "Hoarse since operation." Laryngoscopy, general laryngeal inflammation.

5th week. Cords only remain inflamed.

9th week. Inflammation gone, but there was a fine band of relatively fixed tissue in the interarytenoid region, lying as a semi-circle at, or just below, the vocal processes (fig. 2). Hoarse still, and dyspnœa now.

14th week No change. Did not attend again.



Case 3. Female, aged 53. 21st June, 1949. Abdomino-perineal resection, for carcinoma of the rectum.

2nd day. Mouth and throat sore.

4th day. Dyspnœa, thought to be pulmonary.

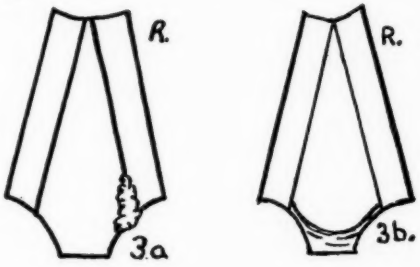
17th day. "Hoarse since operation." Laryngeal roughness and granulation (fig. 3a).

11th week. Laryngeal examination negative, apart from slightly impaired abduction. Voice poor.

16th week. On abduction a web was visible in the interarytenoid region, immediately below the glottis (fig. 3b). Possibly some limitation of movement at the cricoarytenoid joints. Severe dyspnœa on climbing stairs, inspiratory stridor even when seated. Laryngeal airway appeared adequate for ordinary purposes.

12th month. Web thinner and abduction better. Breathing improved.

28th month. Web still present, airway looked adequate. Still some stridor.



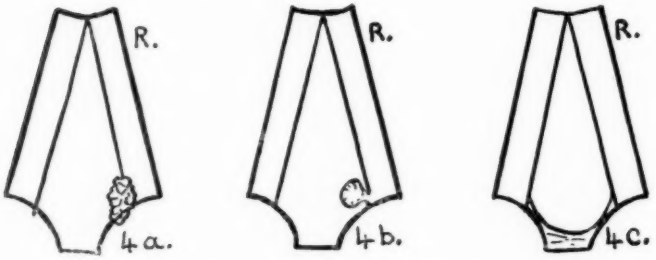
Case 4. Female, aged 47. 28th June, 1949. Partial gastrectomy for carcinoma of the stomach.

5th week. "Hoarse since operation". A small bunch of granulations (fig. 4a).

9th week. A well-defined permanent-looking nodule (fig. 4b). Still hoarse.

16th week. Nodule not seen, but a subglottic scar or web seemed to be forming, so that abduction was incomplete (fig. 4c). The web persisted. It was noticed later that the voice was squeaky rather than hoarse; that the web did not interfere with the cord movement; but at the 36th week, the considerable dyspnœa was more than might be expected from the appearances.

18th month. Appearance unchanged. Breathing better.



Case 5. Female, aged 44. 10th August, 1949. Pan-hysterectomy.

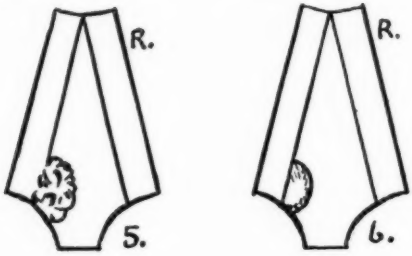
5th week. "Hoarse since operation". Pale polypoid mass (fig. 5).

9th week. Node looked fibrous.

14th week. Removal of nodule. Microscopy: "Capillary angioma, containing areas of haemorrhage."

16th week. Larynx appeared normal. Voice improved.

25th week. Voice still rough. Appearances normal.



Case 6. Female, aged 61. 10th August, 1949. Laparotomy for duodenal ulcer, appendicectomy, taking two hours.

2nd day. Some pyrexia, cough, and sputum; no chest signs.

3rd day. Respiratory distress and stridor, cyanotic. A fleeting glimpse showed the whole laryngeal chamber to be fiery red, much more inflamed than the usual simple acute laryngitis, and the cords to be immobile. Failure of abduction seemed to be the cause of her dyspnœa. There was no œdema. An urgent tracheostomy had to be made, and relieved the distress. Tube removed ten days later.

17th day. Laryngeal appearance that of simple acute laryngitis; one could not be sure that the cords were moving properly.

24th day. Larynx appeared normal. Voice variable.

9th week. A pale polypoid subglottic mass (fig. 6). Slight huskiness.

12th week. Appearance unchanged.

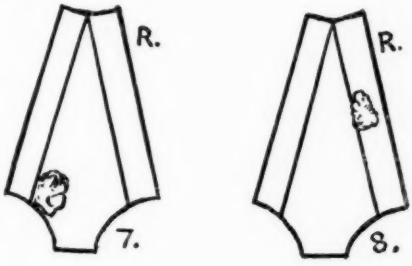
16th week. Surprisingly, the larynx appeared normal. Voice had been normal for some time.

32nd week. Larynx and voice normal.

Case 7. Female, aged 35. 12th July, 1950. Hysterectomy.

13th week. "Hoarse since operation". A soft polypus, pedunculated, and arising from just below the posterior end of the left cord (fig. 7).

5th month. Polypus removed. Microscopy: "Fibrosis and granulation tissue."



Case 8. Female, aged 45. 8th day before operation. Routine laryngoscopy normal. 12th December, 1950. Thyroidectomy for toxic goitre.

7th week. Routine postoperative laryngoscopy: white "Papilloma" on centre of right cord (fig. 8). No symptoms.

12th week. Nodule removed. Microscopy: "a small nodule with thickened epithelium, superficial ulceration, and subepithelial hæmorrhage."

5th month. Larynx apparently normal; voice much improved.

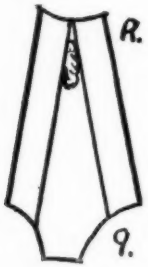
12th month. Voice slightly husky. Laryngeal mucosa not quite smooth.

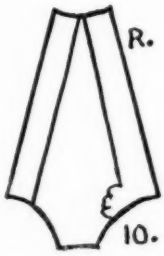
Case 9. Female, aged 34. 7th day before operation. Routine laryngoscopy normal. 5th February, 1951. Partial thyroidectomy for non-toxic goitre.

5th month. Left cord immobile near the mid-line.

8th month. Left cord still immobile, now a pale polypus is flapping from beneath the extreme anterior end of the left cord (fig. 9).

11th month. No change. She is comfortable and does not desire operation

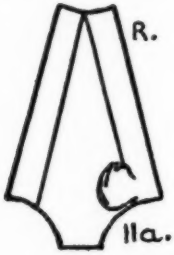




Case 10. Female, aged 31. 10th day before operation. Routine laryngoscopy, normal. 25th May, 1951. Subtotal thyroidectomy, for toxic goitre.

8th day. Routine postoperative laryngoscopy: a small polypoid swelling at the posterior end of the right cord (fig. 10). No symptoms.

25th day. Larynx normal.



Case 11. Female, aged 40. 19th May, 1951. Left fenestration operation.

13th week. "Hoarse for three weeks, voice comes and goes".

Smooth, bluish, rounded tumour the size of a pea, attached to the upper surface of the right cord (fig. 11a).
16th week. Appearance unchanged.
5th month. Small remnant (fig. 11b).
7th month. Larynx and voice normal.

Case 12. Female, aged 50. 2nd day before operation. Routine laryngoscopy, normal.
17th October, 1951. Partial thyroidectomy for toxic goitre.
5th day. Small white nodule on right cord (fig. 12).
6th day. Larynx normal.

SUMMARY

A short account of lesions about the glottis following endotracheal anæsthesia is presented, with a brief summary of twelve cases.

The sequence appears to be, abrasion or hæmatoma, infection, ulceration, granulation; organization to a firm nodule or web-cicatrix. The symptoms may be negligible or serious, dyspnœa sometimes limiting the patients activities, and in one case necessitating tracheostomy. Treatment will depend on the requirements of the individual case.

We wish to thank Professor Victor Lambert, Director of the Department of Otolaryngology at the Victoria University of Manchester, for his helpful criticism of this paper.

REFERENCES

Clausen, R. J. (1932). *Proc. R. Soc. Med.*, **25**, 1507.
Crispell, L. S., and Hampton, L. G. (1950). *Conn. med. J.*, **14**, 98.

Dwyer, C. S., Kronenberg, S., and Saklad, M. (1949). *Anesthesiology*, **10**, 714.

New, G. B. and Devine, K. D. (1949). *Ann. Otol., etc., St. Louis*, **58**, 548.

ADDITIONAL REFERENCES

Baron, S. H. and Kohlmoos, H. W. (1951). Laryngeal sequelæ of endotracheal Anæsthesia, *Ann. Otol., etc., St. Louis*, **60**, 767.

Barton, L.W. (1947). Granuloma of the larynx; a late complication of endotracheal anæsthesia, *Ann. Otol., etc., St. Louis*, **56**, 191.

Cohen, M. (1938). Tumour of the vocal cord following nasal endotracheal anæsthesia, *Brit. med. J.*, **1**, 283.

Farrior, J. B. (1942). Contact ulcer of the larynx developing after intratracheal anæsthesia, *Arch. Otolaryng., Chicago*, **36**, 238.

Flagg, P. J. (1951). Incidence and control of trauma accompanying endotracheal anæsthesia, *Arch. Otolaryng., Chicago*, **53**, 439.

Gould, R. B. (1935). Laryngeal granuloma following intratracheal intubation, *Brit. med. J.*, **2**, 499.

Hill, F. T. (1948). Granuloma following endotracheal anæsthesia, *Ann. Otol., etc., St. Louis*, **57**, 910.

Jackson, C. and Jackson, C. L. (1935). Contact ulcer of the larynx, *Arch. Otolaryng., Chicago*, **22**, 1.

Kearney, H. L. (1946). Bilateral granuloma of the larynx following intratracheal anæsthesia, *Ann. Otol., etc., St. Louis*, **55**, 185.

McLaurin, J. W. (1947). Bilateral granuloma of the larynx following endotracheal anæsthesia, *Laryngoscope, St. Louis*, **57**, 796.

el Mofti, A. (1949). Laryngeal polypoid growths following endotracheal anæsthesia; report of two cases, *J. Laryng.*, **63**, 759.

Moulden, G. A. and Wynne, R. L. (1951). Post-anæsthetic granuloma of the larynx, *Brit. J. Anæsth.*, **23**, 92.

el Samma, E. el Din (1950). Polypoid granuloma of the larynx following endotracheal anæsthesia: report on two cases, *J. R. Egypt med. Ass.*, **33**, 912.

Smiley, W. A. (1940). Polypoid granuloma of the larynx following endotracheal anæsthesia, *Ann. Otol., etc., St. Louis*, **49**, 556.

Tuft, H. S. and Ratner, S. H. (1947). Laryngeal polypoid granuloma following intratracheal anæsthesia, *Ann. Otol., etc., St. Louis*, **56**, 187.

Wattles, M. (1949). Bilateral granuloma of the larynx following intratracheal anæsthesia, *Ann. Otol., etc., St. Louis*, **58**, 873.

Wright, W. K. (1951). Bilateral contact ulcer granuloma following endotracheal anæsthesia, *Arch Otolaryng., Chicago*, **53**, 670.

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CHEMICAL CONTROL OF SODA-LIME EFFICIENCY IN CIRCLE FILTERS

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"PRIMUM NON NOSCERE" continues to be one of the most important aphorisms—if not the most important of all—in contemporary medicine and anæsthetists should never ignore it. The use of elaborate anæsthetic technique entails correlated dangers, which can only be counteracted by minute and profound knowledge of the situation created.

Under this heading comes closed circuit respiration, which to-day is so commonly employed that its handicaps are often forgotten. Facilities in blood and plasma transfusion, which frequently accompany good anæsthetical organisation, are capable of disguising many misuses of carbon dioxide absorbers.

To ventilate a patient with oxygen is ordinarily a simple matter, but the adequate removal of carbon dioxide may be neglected. In fact, the criteria relied upon to assess the efficiency of carbon dioxide absorption are not entirely satisfactory for the following simple reasons:

1. The best brands of soda-lime when stale produce misleading results. For example, in the hospital stores, the container that was last bought can be incorrectly arranged in front of formerly acquired ones, so that the anæsthetists may later use a very stale soda-lime, supposing it to be fresh. This is more liable to occur in hospitals which buy in bulk. The situation is worse in many countries which must import soda-lime, a painfully long procedure,

currently taking many months; the result is that the soda-lime, when finally put in the canister, is no longer fresh, and fails to absorb efficiently from the very beginning of its use.

2. When the operating-room temperature is unusually low or high, or the anæsthesia is of short or medium duration, or the patient, owing to his metabolic peculiarities, produces too little or too much CO_2, the canister temperature, as judged by the hand, cannot be considered an accurate guide.

3. "Indicating" soda-lime is useful only in transparent containers, and even then gross mistakes can occur (Adriani and Rovenstine, 1941; Adriani, 1946).

4. Last and most important, it is neither consistent nor ethical to propose removing the exhaled CO_2 by means of a special technique, and afterwards await the appearance of evident clinical signs of CO_2 excess (or intoxication) before changing the soda-lime. In fact, when the patient himself exhibits respiratory and/or circulatory symptoms of CO_2 accumulation, the anæsthetist is definitely in the invidious position of correcting something which he formerly proposed to avoid. In other words, he used his patient as a biological test of the soda-lime! It is likely that if the patients were asked permission beforehand to allow themselves to be used in this way, many, if not all, would prefer some other less elaborate anæsthetic technique!

Most patients are very responsive in their natural reflexes and so the symptoms of CO_2 accumulation are very evident. On the contrary, other patients, such as those in pre-operative and anæsthetic pending or established shock, or in fluid imbalance, are partially incapable of exhibiting the normal respiratory and circulatory responses to CO_2 accumulation.

Many authors have demonstrated that the signs of CO_2 accumulation are less evident in the anæsthetized patient and diminish as the narcosis becomes more and more profound (Comroe and Schmidt, 1938; Leigh, 1942; Moyer and Beecher, 1942; Seevers, 1944; Draper, Whitehead, and Spencer, 1947; Dripps, 1947; Roth, Whitehead, and Draper, 1947), a point being reached when the three reflexes which act as a guide to the anæsthetist are not stimulated, even by high CO_2 tensions (Courville, 1941; Editorial, *Anesthesiology*, 1942; Guedel, 1944; Krichin and Shkurman, 1947; Evans, 1949).

At this point it is necessary to remember the well-established fact that CO_2, above certain concentrations, acts as a depressant agent (Seevers, 1944).

Matters become more complicated when we take into consideration the techniques of controlled respiration, total curarization, and controlled hypotension: patients under these forms of anæsthesia can exhibit neither the respiratory nor the circulatory symptoms of CO_2 accumulation for obvious reasons and so, without warning, they pass into gaseous acidosis with all its consequences. An example is the so-called " cyclopropane-shock ".

It would appear that the usual mistake concerning soda-lime is not to change it when necessary. The converse mistake, which has fortunately only economical consequences, is to discard absorbing material. This probably happens most often during painful interventions performed under light narcosis but not accompanied by regional block, since the signs which then appear resemble those of CO_2 accumulation.

On the whole, it can be said that concentrations of CO_2 under 0.5 per cent are innocuous and can be tolerated for long periods in spite of the fact that the normal content of fresh air is of the order of 0.04 per cent. This figure of

0.5 per cent was established by physiological, hygienic and pharmacological studies. Of course, for short periods, concentrations of CO_2 higher than 0.5 per cent may also be tolerated.

When using to-and-fro absorbers it is very difficult to measure the CO_2 content of the inhaled mixture, because there exists a fluctuating equilibrium between the CO_2 excretion by the patient and absorption by the soda-lime, approximately in the reverse manner to the equilibrium which exists between the fresh O_2 entering through the inlet and the oxygen absorbed by the patient. The exact conditions which exist in these circumstances remain obscure and very little more is known than that—as time goes on—the respiratory dead space (at least as far as CO_2 is concerned) increases at every moment.

In the circle absorber, on the other hand, it is possible to measure the CO_2 concentration of the inhaled mixture. For this purpose the writer has employed the "Carbon Dioxide Detector" developed by William B. Draper in 1939 and furnished by Ohio Chemical and Manufacturing Company under the name "Hi-CO Detector" (Draper, 1939).

This simple accessory consists of two ball valves, two bubble tubes, two test tubes (equipped with tightly fitting rubber connections) and a rubber bulb mounted in series with the inspiratory side of the circle absorber (figs. 1 and 2).

Squeezing the rubber bulb closes one of the valves, lifts the other and the air from the bulb passes into the respiratory circuit. When the bulb is released, its natural elasticity creates a negative pressure, which has a reverse effect on the valves, so that the final result is the bubbling of a sample of inhaled mixture through the test tubes. The first

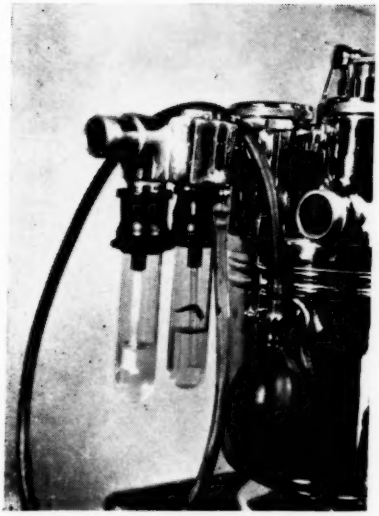

FIG. 1

The Carbon Dioxide Detector connected to a circle filter.

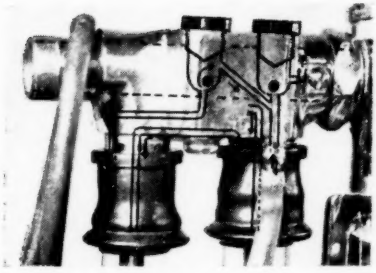

FIG. 2

Semi-diagrammatic representation of the channels inside the Carbon Dioxide Detector.

test tube contains tap water to retain soda-lime dust, and the second one the chemical reagent used in the test.

This apparatus *per se* does not open the closed circuit nor increase the resistance to respiration.

The chemical reagents used for CO_2 estimation may be divided into two main groups:

1. Reagents which simply detect the presence of H_2CO_3 by turbidity according to the following equations:

$$H_2CO_3 + Ca(OH)_2 = 2H_2O + CaCO_3 \downarrow$$
$$H_2CO_3 + Ba(OH)_2 = 2H_2O + BaCO_3 \downarrow$$

When gas containing low concentrations of CO_2 is bubbled through these reagents, the clear solution becomes milky.

2. Reagents which identify pH alterations caused by H_2CO_3 by colour changes in chemical indicators.

Theoretically, since it is intended to estimate a weak acid, the only useful chemical indicators are those with a critical point near neutrality. A list of these appears in table I. A very weak alkaline solution containing any of the chemical indicators quoted may be used in the test.

The chemical reagent having been prepared, it is of the utmost importance to calibrate its sensitivity.

TABLE I

Colour changes in chemical indicators suitable for the estimation of CO_2

pH indicator	Colour	pH	Colour
Phenosulphonphthalein	Yellow	6.8–8.4	Red
Rosolic Acid	„	6.9–8.0	„
Cresol Purple	„	7.2–8.8	„
Metacresol Purple	„	7.4–9.0	Purple
Tropeolin 000	„	7.6–8.9	Rose
Thymol Blue	„	8.0–9.6	Blue
Cresolphthalein	No colour	8.2–9.8	Red
Phenolphthalein	„	8.3–10.0	„

SENSITIVITY TESTING

For this purpose the anæsthetic machine is used, with the CO_2 detector already connected, and various O_2-CO_2 flows are employed. If the flowmeters are correctly calibrated (some small variations are unimportant) a flow of, for instance, 50 ml. of CO_2 and 10 litres of O_2 per minute will contain approximately 0.5 per cent of CO_2. With this O_2-CO_2 mixture flowing, the rubber bulb is squeezed a number of times, an interval being permitted between the successive squeezes. It is very simple to observe the characteristic changes which occur in the chemical reagent at the completion of a certain number of squeezes of the rubber bulb.

We have tried and tested the following reagents:

1. A clear filtered solution of 40 g. of $Ca(OH)_2$ in 500 ml. of distilled water. Weak but evident turbidity was considered the characteristic change of this reagent.

2. Saturated (at 15°C) clear filtered solution of $Ba(OH)_2$ in distilled water. Weak but evident turbidity was considered the characteristic change of this reagent.

3. NaOH 0.0005N with phenolphthalein *quantum satis* to a characteristic purple colour. Complete discolouring was considered the characteristic change.

4. 0.04 per cent solution of Bromothymol Blue with sufficient 0.01N NaOH added to develop the typical blue colour. A complete change to yellow was considered the characteristic end point.

In a number of sensitivity tests we obtained the results in table II.

The chemical reagents of the second group are, on the whole, difficult to manage because it is necessary to use laboratory accuracy (neutral glass, frequent re-testings, neutral washings of the test tubes, etc.).

TABLE II

Calibration of percentage of CO_2 against number of squeezes of the bulb with various indicators.

CO_2%	$Ca(OH)_2$	$Ba(OH)_2$	Phenolphthalein	Bromothymol Blue
10	1 squeeze	1 squeeze	1 squeeze	1 squeeze
5	1 „	1 „	1 „	1 „
2	1 „	1 „	1 „	1 „
1	2 squeezes	1 „	2 squeezes	3 squeezes
0.5	6 „	1 „	2 „	10 „
0.25	12 „	2 squeezes	4 „	?
0.10	40 „	4 „	20 „	?

In anæsthetic practice the writer uses only the $Ca(OH)_2$ solution which is less expensive, easily prepared and tested, and sufficiently accurate.

One condition for accuracy is always to put the same quantity of the same reagent in the same test tube, squeezing the rubber bulb with the same strength.

PROCEDURE DURING ANAESTHESIA

During the administration of an anæsthetic, from time to time we squeeze the rubber bulb of the carbon dioxide detector. If the soda-lime is absorbing well, some turbidity appears after many squeezes, because soda-lime does not absorb CO_2 completely (Adriani and Rovenstine, 1941). Each time that there appears turbidity, an equal quantity of fresh reagent is substituted in the test tube and the process begins again. As the soda-lime begins to absorb less efficiently the characteristic change appears after fewer squeezes. It thus becomes evident, beyond any doubt, that the CO_2 content of the inhaled mixture is increasing. Since the reagent has already been calibrated we know exactly how many squeezes correspond to 0.5 per cent of CO_2. By this means, the CO_2 content of the inhaled mixture is determined within an accuracy of one half per cent, an accuracy which is completely satisfactory for clinical purposes.

We have, since 1946, performed tens of thousands of these estimations in circle filter apparatus and we are completely convinced that soda-lime absorption presents no problems with this type of chemical control.

REFERENCES

Adriani, J., and Rovenstine, E. A. (1941). *Anesthesiology*, **2**, 1.
Adriani, J. (1946). *The Chemistry of Anesthesia*, Springfield: Thomas.
Comroe, J. H., Jun., and Schmidt, C. F. (1938). *Amer. J. Physiol.*, **121**, 75.
Courville, C. B. (1941). *Anesthesiology*, **2**, 46.
Draper, W. B. (1939). *Patent U.S.*, **2**, 136.
——Whitehead, R. W., and Spencer, J. N. (1947). *Anesthesiology*, **8**, 524.
Dripps, R. D. (1947). *Anesthesiology*, **8**, 15.
Editorial (1942). *Anesthesiology*, **3**, 83.
Evans, F. T. (1949). *Modern Practice in Anæsthesia*, London: Butterworth.
Guedel, A. E. (1944). *Inhalation Anesthesia—A Fundamental Guide*, New York: Macmillan.
Krichin, D. G., and Shkurman, P. O. (1947). *Vrach. Delo.*, **27**, 23.
Leigh, M. Digby (1942). *Anesthesiology*, **3**, 429.
Moyer, C. A., and Beecher, H. S. (1942). *J. Urol.*, **48**, 222.
Roth, L. W., Whitehead, R. W., and Draper, W. B. (1947). *Anesthesiology*, **8**, 294.
Seevers, M. H. (1944). *N.Y. St. J. Med.*, **44**, 597.

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SPASM OF THE BRACHIAL ARTERY TREATED BY BRACHIAL PLEXUS BLOCK

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IN the presence of an embolus, spasm of a vessel should not be relieved before embolectomy, lest the embolus dislodges itself and becomes unapproachable to surgery, or lodges itself in a more vital part of the body. However, in the case to be described, in view of the patient's grave condition, local anæsthesia was imperative. This relieved the spasm of the brachial artery and cured the arm.

Mrs. E. G., age 74, was admitted to hospital with a history of sudden onset of severe pain, glove paræsthesia of the right arm, and paralysis of her fingers, which became discoloured six hours before admission.

On examination she was found to be very ill, suffering from congestive heart failure and auricular fibrillation. Her right arm was cold, almost white, and anæsthetic to pin prick from the elbow down to the tips of her fingers. There was paralysis of the interosseous muscles of the hand, and no radial or brachial pulsation could be detected. Calcification of her arteries was obvious. Diagnosis of an embolism with severe spasm of the radial artery was made. Treatment with heparin 10,000 units four hourly and digitalis therapy was commenced. The patient was taken to the theatre for embolectomy. General anæsthesia was definitely contra-indicated in view of the patient's grave condition. A right anterior brachial plexus block was performed using 15 ml. of 1 : 1000 amethocaine. Within twenty minutes and before the operation was due to start, the

patient began complaining of an unpleasant sensation in the arm. The colour of the arm improved and pulsation of the radial and brachial artery, though feeble at first, could be felt. The patient was sent back to the ward without undergoing operation. One hour later, the colour of the arm and the radial pulsation were normal, and the movements of the fingers returned. In view of the patient's cardiac condition she was kept in hospital for three weeks. When she was discharged her right arm was normal.

This could be a case of simple spasm of the brachial artery with no obvious ætiology and successfully relieved by the block. The presence of congestive cardiac failure and calcification of the brachial artery, however, made it likely that the spasm was initiated by a small clot which was held up *in situ* by the narrowing artery. When the spasm was relieved by brachial plexus block, the embolus was free in the lumen of the brachial artery, and carried by the blood to a more distal part of the arm, finally lodging itself in a smaller artery, where adequate collateral circulation prevented anoxia of the tissues.

It is of interest that local injection of anæsthetic drugs or periarterial sympathectomy is seldom successful in relieving the spasm, whereas nerve block is more reliable. Vaso-dilator drugs such as papaverine hydrochloride gr.$\frac{1}{2}$ (30 mg.) in repeated doses may be very useful adjuvants to the nerve block.

John Snow.

Reproduction of John Snow's bookplate, by courtesy of Professor R. R. Macintosh.

ON THE

INHALATION

OF THE

VAPOUR OF ETHER

IN

SURGICAL OPERATIONS:

CONTAINING A

DESCRIPTION OF THE VARIOUS STAGES OF ETHERIZATION,

AND

A STATEMENT OF THE RESULT OF NEARLY EIGHTY OPERATIONS IN WHICH ETHER HAS BEEN EMPLOYED IN ST. GEORGE'S AND UNIVERSITY COLLEGE HOSPITALS.

BY

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LECTURER ON FORENSIC MEDICINE.

LONDON:
JOHN CHURCHILL, PRINCES STREET, SOHO.

1847.

PREFACE

FROM questions addressed to me by medical visitors and students, after the operations in the two hospitals in which I have had the honour of frequently administering the ether, I judged that a fuller account than I had hitherto given of the process might be useful and not unacceptable to many members of the profession, and that there would be some advantage in presenting it in a separate form, although, as a general rule, the medical periodicals and transactions of societies offer the best medium for communications of moderate length like the present.

I have treated as briefly as I could, in the following pages, of the chief application only of the great discovery that will render last winter a memorable epoch in the annals of medical science. I have not even alluded to the use of the vapour of ether in medicine or midwifery, and I have not entered on the relations of etherization to medical science or physiology, although there is a tempting field for research; for the power we have acquired, through the discovery of our medical brethren in America, of inducing at will and with perfect safety such a state of insensibility as we should previously have thought to be alarming, cannot be without its influence on the progress of our knowledge of the diseases of which insensibility forms a symptom, and of the functions of the nervous system generally.

The remarks in the text are confined strictly to the practical part of the subject, and a few explanatory notes that seemed to be required are placed in a short appendix.

The inhalation of ether will, no doubt, have superior works to the present dedicated to its elucidation before long, not only from increase of knowledge respecting it, but from improved ways of treating on it, for it is not easy to reduce a new branch of science to suitable language in the first attempts.

54, FRITH STREET, SOHO SQUARE.
September, 1847.

ON THE

INHALATION

OF THE

VAPOUR OF ETHER

IN

SURGICAL OPERATIONS

THE point requiring most skill and care in the administration of the vapour of ether is, undoubtedly, to determine when it has been carried far enough. In order to communicate, with some degree of clearness, what I have been able to observe by close attention to the subject, I shall divide the effects of ether into five stages or degrees; premising, however, that the division is, in some measure, arbitrary,—that these different degrees run gradually into each other, and are not always clearly to be distinguished, —and that the language I have used has been chosen with the sole object that my meaning might not be mistaken.

In the first degree of etherization I shall include the various changes of feeling that a person may experience, whilst he still retains a correct consciousness of where he is, and what is occurring around him, and a capacity to direct his voluntary movements. In what I call the second degree, mental functions may be exercised, and voluntary actions performed, but in a disordered manner. In the third degree, there is no evidence of any mental function being exercised, and consequently no voluntary motions occur; but muscular contractions, in addition to those concerned in respiration, may sometimes take place as the effect of the ether, or of external impressions. In the fourth degree,

no movements are seen except those of respiration, and they are incapable of being influenced by external impressions. In the fifth degree, (not witnessed in the human being), the respiratory movements are more or less paralysed, and become difficult, feeble, or irregular.

If a middle-aged man, of about the average size, is supplied with air mixed with vapour of ether, in the proportion of 45 per cent. vapour to 55 per cent. air, and breathes it easily and without obstruction, he usually consumes about two drachms of ether per minute. It is not all absorbed, for a part is expired after passing no farther than the trachea. At the end of the first minute he is usually in the first degree of etherization; of the second minute, in the second degree; of the third minute, in the third degree; and at the end of four minutes, having inhaled an ounce of ether, in the fourth degree. If the inhalation is now discontinued, he commonly remains in this degree of etherization for one or two minutes, passes gradually back into the third degree, which lasts for three or four minutes, at the end of which time he is in the second degree, which lasts about five minutes, to give place to a feeling of intoxication and exhilaration, which lasts for ten or fifteen minutes or longer before it entirely subsides.

Having thus sketched an outline of the process of etherization, we may now proceed to examine the different states of it a little more closely.

Generally, all that the patient remembers of the effects of ether occurs whilst he is under its influence in the first degree only, and his feelings are usually agreeable—often highly so. I consider that it is not practicable to perform operations, in the absence of pain, without carrying the effects of ether further than this degree. Whilst the effect of the ether is going off, however,—after persons have been completely insensible,—they are not unfrequently free

from the pain of an operation, which is still going on, at a time when the mental faculties have returned, together with the special senses of sight and hearing, and when they are consequently in what I have denominated the first degree. Of this degree, as it follows the others, we shall have to speak again. If etherization is not carried further than this degree it quickly subsides, without leaving any appreciable effects; but if the inhalation is continued, the second degree succeeds to this.

When the ether is administered in the method that I recommend, the patient usually passes quietly and quickly through the second degree of etherization without its being manifested in any way. As he is not questioned, the state of his mental faculties does not appear, and he passes rapidly into the next degree. Sometimes, however, when from the tendency of the vapour to produce coughing it is given in a more diluted form than usual, and occasionally, also, from peculiarity of constitution, this degree of the effect of ether is made apparent by gesticulation, words, or attempts to move; and in hysterical females, sometimes by sobbing, laughing, or screaming. The patient often tries, by lifting up his hands or moving his head, to remove the inhaler from his face whilst in this stage. He feels something there interfering with his ordinary respiration, and the purpose and nature of it have passed from his mind; his endeavours are voluntary, but guided by instinct rather than reason. He can often be quieted by language addressed to him, and will do as he is bid, although unconscious of where he is,—as his answers, if he makes any, shew. At other times he is obstinate, or regardless of what is said. I believe that all the dreams which patients have when taking ether, occur only whilst they are under its influence in this degree. If the ether is discontinued at this stage of the inhalation, the patient goes back into the first degree,

either immediately or in the course of a few minutes, according to the extent he has advanced, or the time he has been kept in this degree. According to what I have seen, a surgical operation would cause pain, if etherization were not carried farther than this degree, although, if the pain should not arouse the patient and bring him back to the first degree, he would probably not remember it. But it would be more difficult for the surgeon to operate with this amount of etherization than without ether.* It appears that surgical operations have often been performed in this stage, and several eminent surgeons were at one time opposed to the use of ether, on account of the struggling which they supposed to be inseparable in most cases from operations performed under its effects.

When the patient has been more deeply etherized, he is often totally insensible to a surgical operation, as the effect of the ether is going off, whilst he is under its influence only to the second degree. Of this we shall speak below.

To proceed to the third degree. It is stated above that if the patient moves or struggles, when under the influence of ether in the second degree, his movements are guided by volition, though not by knowledge or reason; but if he struggles in the third degree of etherization his movements are not voluntary, any more than the struggling in hysteria or epilepsy. Usually, however, there is no struggling. The patient may have moved his eyes about in the second degree, and even directed them to objects, but in this degree they are stationary, or if they do move, their motions have

* From accounts that I have heard of two or three cases, it seems probable that if the patient were kept for some time in this stage of etherization, by breathing very diluted vapour, an immunity from pain might in some cases result; and this is corroborated by an observation I made on a bird, which had been for ten minutes in an atmosphere containing ten per cent. of vapour of ether; but it is not likely that such a plan of administering ether would generally succeed, or be so good as that usually adopted.

nothing of a voluntary character. They are sometimes turned upwards as in sleep, but I think not so frequently as in the next degree. The eyelids may be either open, or partly or tightly closed, but in either case, if lifted or moved by the finger, the orbicularis palpebrarum contracts. The breathing is usually regular and somewhat deep; the patient lying still, or, if sitting, having a tendency to slide out of the chair; but occasionally the limbs are rigidly contracted, and when this is the case the patient sometimes holds his breath for several seconds at a time. He may moan in this degree of etherization, but never gives utterance to articulate sounds, which are always an indication that he has not advanced farther than the second degree, or has returned to it. Therefore the performance of a surgical operation in this stage would not cause a person to cry out in articulate sounds, unless it roused him, and caused him to return to the second degree; it might, however, cause him to groan and flinch. If this degree is well established, and if the patient has been detained in it, at the same point, by inhaling at intervals, or by inhaling dilute vapour, an operation may usually be performed without producing any other effect than a distortion of the features expressive of pain, and, perhaps, a slight moaning, and an increased frequency of respiration, and, in some instances, a general rigidity of the muscular system. If this degree of etherization is not well established when the operation begins, the first cut may cause a sudden contraction of the whole muscular system. Persons in a full state of health, and more particularly those in a state of plethora, are much more liable to struggling and rigidity in this degree, than those whose strength is reduced by illness; and if from any cause the supply of atmospheric air is limited, and something of asphyxia is combined with etherization, I believe that the struggling is more liable to occur,

and is more severe. There is never any recollection of operations in this degree, even when symptoms of pain have been exhibited, and there is scarcely ever, I believe, any sign of pain in this degree, when it succeeds to the fourth, as the influence of the ether is subsiding. If the exhibition of ether is discontinued in the third degree, the patient goes back into the second degree immediately, or in the course of two or three minutes.

In the fourth degree all the muscles are relaxed, and the limbs hang down, or rest in any position in which they are supported. The eyelids fall down over the eyes, or remain as they are placed by the finger. The eyes are either turned up or remain central. The breathing is deep, regular, and automatic, and there is often snoring. The muscles of the face partaking in the general relaxation, the countenance is devoid of expression, having a placid appearance as in a sound sleep. Sometimes the lower jaw has a tendency to droop; the mouth is partly open, and the features are so relaxed, that the countenance is altered, and has the vacant appearance seen in paralysis, idiocy, or a helpless state of drunkenness; and if there is at the same time snoring and blowing of the lips in respiration, as now and then happens, an appearance is met with that would be truly alarming, if we did not know that it was only due to an agent which is flying away every moment in the breath, to leave the patient, in a few minutes, without any permanent trace of its having been there. In this degree of etherization the patient always remains perfectly passive under every kind of operation; and as the muscles are completely relaxed, this is the proper stage for the reduction of dislocations. The patient never begins to snore until he has reached the fourth degree, or is passing into it from the third, and from all that I have hitherto observed, I believe that when he snores from the effects of ether, he

is always totally insensible to every thing which is done to him. This degree of etherization seldom continues more than two or three minutes after the process of inhalation is left off, and I have never kept the patient in this stage more than five or ten minutes; but in operations of long duration have allowed the effects of the vapour to diminish somewhat from time to time. The integrity of the functions of respiration and of circulation is not impaired in this degree. The breathing is generally deeper than usual, and although it has been somewhat stertorous in two or three instances, yet it continued with great regularity, and the stertor subsided in a minute or two. The pulse is distinct and of good volume, even in patients affected with hectic, in whom, just before the inhalation, it was small and hard. It is usually accelerated, as in all the other stages of etherization. The sensibility of the glottis and pharynx continues in this degree, for the blood which flows backwards in operations on the nose and mouth is all swallowed, none of it getting into the trachea.

In the fifth degree, as met with in animals inferior to man, they remain motionless and flaccid as in the fourth degree, and respiration begins to be irregular, feeble, or laborious. The muscles of respiration begin to suffer the loss of power which already involved the merely voluntary muscles. The sensibility on which respiration depends, and which has outlasted the special senses and common sensibility, now begins to be abolished under the effects of an increased quantity of ether. This is the stage immediately preceding death when animals are killed by ether, and there can be no doubt that it would be met with in the human being, if the vapour were exhibited so as to increase its effects to a dangerous degree beyond what is ever required (1).* However nearly dead animals may be from ether, if

* The numbers refer to the Appendix.

the breathing has not actually ceased when the vapour is discontinued, they always recover, as was stated by the author, at the College of Physicians, when he had the honour of performing some experiments at the conclusion of Dr. Wilson's Lumleian Lectures, on the subject of Pain, in March last. This circumstance illustrates forcibly the great safety of the inhalation of ether, and how much it differs in this respect from asphyxia, and the exhibition of narcotics by the stomach.

The fifth degree of etherization has only been mentioned as a state to be avoided, and we proceed now to the degree which follows the fourth, when the patient is no longer kept in it; and this is the third degree, as it appears a second time. It is usually less marked now than when it preceded the fourth degree, and struggles and rigidity are less frequent,—seldom, if ever, taking place except they have previously occurred in the same degree, and not by any means constantly, when such has been the case. If struggles do occur, and especially if they are accompanied by moaning, as sometimes happens, and if a surgical operation is going on, it may appear to an inattentive observer that the patient is feeling pain, when such is not the case; for a closer attention will shew that the supposed signs of pain are not increased when cuts are made, or ligatures tied on the arteries; and if the ether is not re-administered, and the patient is allowed to recover still further during the operation, it will probably happen that in the second degree he will either lie perfectly calm, or talk in his dreams about subjects totally unconnected with pain, or the operation which is still going on. And it is not to be supposed that he is becoming less sensible as the effects of the narcotic are subsiding. I believe that pain is seldom felt in the stage of which we are treating—the third degree succeeding the fourth—and of course never remembered afterwards,

as there is no knowledge or mental perception of it. This stage of etherization seldom lasts longer than from two to four minutes before it gives place to the second degree, if the inhalation is not resumed.

The second degree is usually much better marked as the patient is recovering from the ether, than when he is getting under its influence; it also lasts much longer at this time, the reason of which is obvious; for when he is inhaling the vapour he is quickly removed from this into the third degree, but when the inhalation is discontinued the vapour is got rid of, in a ratio varying directly with the quantity in the blood, which is a constantly decreasing ratio. The blood, in passing through the capillaries of the lungs, shares its ether with the air taken into the air cells, and, consequently, the process of de-etherization becomes slower as it goes on (2). For this reason, also, this degree continues longer than the third, often lasting five minutes, and occasionally more than twice that period. The dreams which patients so often say that they have had during the operations, take place, I believe, only in the second degree of etherization; and generally in the recurrence of this degree, as the effects of the ether are subsiding, and more commonly after than during the operation. If the patient talks, it often happens that what he says is in accordance with what he afterwards remembers of his dreams, which often refer to early periods of his life; and a great number of patients dream that they are travelling. The impression of the length of the dreams can of course be no argument as to how long the person was dreaming, and that impression is often of a longer time than the whole period of insensibility; and I think that there is every reason to presume, that there can be no dreams or ideas of any kind in the third and fourth degrees of etherization, and that for a short time there is not only, as in a sound sleep,

the absence of mental functions, but also the impossibility of their performance. Indeed, from a comparison of what patients sometimes express by words or gestures under the influence of ether, with what they say of their dreams, it would appear that the dreams which are remembered occur only when the patients are fast emerging from the second degree into a state of complete consciousness. Some of the mental states met with in this degree are highly interesting in a psychological view, but the description of them does not form a necessary part of this small treatise. The laughing and crying, which are now and then met with in this degree, are not always the result of joy or sorrow, or even connected with any state of mind corresponding to the expressions, but resemble the laughing and crying of hysteria. The patient is often incapable of pain in the stage which we are considering, but not always so; very commonly he is so in a part of this stage, but if the operation continues he begins to shew signs of feeling it, and the inhalation has to be resumed before he passes into the first degree.

After the patient has recovered his consciousness of surrounding circumstances, there is usually a degree of exhilaration, or some other altered state of the feelings for a little time,—accompanied, sometimes, with a little confusion of the mind, and inability to walk steadily. This, which I have called the first degree of etherization, subsides more slowly than the other degrees, remaining, in some instances, half an hour in a marked degree, and to a slight extent for two or three hours. The patient often expresses his gratitude to his surgeon in more ardent and glowing terms than he otherwise would do if the remaining effect of the ether were not counteracting his usual reserve. Let us hope that *in æthere veritas* is as applicable as the old reading, and that, in these instances, we only witness

the usual feeling of the public towards the medical profession. Commonly, the patient would feel pain if any part of an operation were performed in this stage, but not always; for, in some instances, the special senses of sight and hearing, and complete consciousness and volition, return before common sensibility, and the operation may be going on, for a short time, without his feeling it, and perhaps, whilst he, thinking that it is concluded, is remarking that he did not feel it. But even in these exceptional cases the patient soon begins to complain if the operation continues. Sensation usually, however, remains blunted for some time, and there is generally no smarting in the wound for a little time (often half an hour) after consciousness has completely returned.

The effects of ether were divided into three stages by Dr. Plomley, of Maidstone,* early in the year. The first degree in the above division would include his first two stages, and the next three degrees would be comprised in his third stage. M. Longet † divides etherization into that of the cerebral lobes, and that of the annular protuberance; and M. Flourens makes three degrees as follows: —

"Under the action of ether, the nervous centres lose their powers in regular succession; first, the cerebral lobes lose theirs, viz. the intellect; next, the cerebellum loses its, viz. the power of regulating locomotion; thirdly, the spinal marrow loses the principle of sensitiveness and of motion; the medulla oblongata still retains its functions, and the animal continues to live: with loss of power in the medulla oblongata, life is lost." (Gazette des Hôpitaux, 20 Mars, 1847: quoted in Brit. and For. Med. Rev.)

My second degree corresponds to the etherization of the cerebral lobes of M. Flourens. There are, to be sure,

* Lancet, Jan. 30.

† Archives de Méd., Mars 1847.

occasionally, dreams and indications of disordered intellect, but these could not be recognized in animals, the subjects of his experiments. His next stage corresponds to my third degree; and his last, or the etherization of the spinal marrow, to my fourth degree. The division I have made from observations on patients, will, I think, be found to be better for practical purposes than this, which it very much resembles, of M. Flourens, the result of experiments on dogs; and it involves no theory about the functions of the nervous centres, which is perhaps an advantage, as those, particularly of the cerebellum, are probably not definitively known.

It will be observed, that the non-liability to pain does not correspond uniformly with the state of the patient in other respects when under the effects of ether, and that I have made the division into degrees, according to the other and obvious symptoms, and not according to that which could only be determined by the knife.

The question may be asked, whether the medical man can always determine in what degree of etherization the patient is, and by that means estimate correctly whether or not he is liable to pain. I am not sure that he always can, by the mere observation of the patient. I have never been deceived as to the degree of etherization, but then I always know the strength of the vapour which the patient is breathing, and by observing the length of time that he has been inhaling, and the depth of his inspirations, I know in what stage he ought to be, and am in this way guided in the cases in which well-marked symptoms are absent. In many cases, the moment when an operation may, with propriety, be commenced, is indicated by unmistakeable signs; but, in other instances, it must be acknowledged that the point has to be determined by the consideration and balancing of several particulars. This, however, ought to

be no obstacle; for it is only in this way that the medical man is guided in his usual avocations. His diagnoses and prognoses are generally arrived at by a mental operation of this kind, and not by the observation of some certain sign.

(*To be continued*)

EMINENT ANÆSTHETISTS, No. 8

DUDLEY WILMOT BUXTON

By F. F. CARTWRIGHT
King's College Hospital, London

IN the latter half of the nineteenth century, University College Hospital was the home of progressive anæsthesia. Both John Snow and Joseph Thomas Clover were unofficially attached to the hospital; after Clover's death, D. W. Buxton received the official appointment as anæsthetist. Both Snow and Clover were thinkers and scientists who endeavoured to put the empirical art of anæsthesia upon a scientific footing; their work was continued and brought to fruition by Buxton, for whom it may with justice be claimed that he is very largely responsible for the present position of anæsthesia and its teaching.

Dudley Wilmot Buxton was born on June 28th, 1855, the second son of Harry Wilmot Buxton, Barrister at Law. He was educated privately and then at University College, London; in 1878 he proceeded to University College Hospital. His student career was brilliant and, in spite of the fact that he had to earn his keep by acting as a clerk in his spare time (as did so many nineteenth century medical students), he qualified with distinction in both the Conjoint and M.B. examinations in 1882. Two years later he achieved both his M.D. and the Membership of the Royal College of Physicians.

Meanwhile, Buxton had served both as House Physician and House Surgeon at University College Hospital. His leaning was towards medicine, especially towards experi-

mental medicine. In 1884 he was appointed assistant to Sydney Ringer, Professor of Medicine at University College Hospital; in this year Buxton published the first of his many papers, "Some remarks on the methods of demonstrating the action of certain drugs upon the Frog's heart"; he was also joint author with Ringer of an important paper on the action of acids and alkalies upon the tonicity of the heart and arteries.

Buxton now seemed to be well set upon a successful career as a physician; he had edited the fourth edition of Waring's *Therapeutics* and had been appointed Physician to the Marylebone General Dispensary; but his work with Ringer was to turn his thoughts into other channels. Sydney Ringer's chief experimental work was on the action of drugs upon the heart muscle; the effects produced by the action of chloroform interested Buxton in the practical problems of anæsthesia. His interest, once aroused, was held, and he decided to specialize. In 1885 Buxton was appointed to be the first official anæsthetist on the staff of University College Hospital; later he was appointed to the staffs of the Hospital for Women, the Royal Dental Hospital, and the National Hospital, Queen's Square.

His first paper on the subject of anæsthesia, published in 1885, is interesting, if only for its title. Buxton was a scholar of no mean order, well versed in the Classics; his use of the word "artificial" in his publication "The Practice of Artificial Anæsthesia, Local and General" bears witness to this fact and shows us that he was aware that "anæsthesia" is no modern term, but has a respectable history. In this paper he drew attention to Pean's first observation of a state of true analgesia.

Clover had endeavoured to introduce nitrous oxide into anæsthetic practice and had evolved his nitrous oxide-ether sequence as an answer to the dangers of chloroform. He

met with little success, for the majority of his colleagues regarded the gas as a dangerous agent, owing its action to asphyxia alone; although, it is interesting to note, there was a section of thought which still adhered to Beddoes' and Davy's original theory that the effects of nitrous oxide were due to hyper-oxygenation. Buxton carried on Clover's work; in the years 1886–7–9 he published papers on the action of nitrous oxide and pleaded for its use, in place of the more lethal chloroform, in dentistry and minor surgery. Nitrous oxide may be said, for all practical purposes, to have been introduced by Buxton into anæsthesia in this country, while the continuous nasal method of inhaling the gas was entirely his invention.

Although the story of the "chloroform commissions" has been often told, no account of Buxton's work would be complete without some reference to them and to the part that he played. At this time, chloroform was almost the universal anæsthetic, but it was recognized that mortality was high and was apparently inevitable. In the year 1879, the British Medical Association appointed a commission to inquire into the relative safety of ether and chloroform; the findings of this, the "Glasgow Committee," were wholly unfavourable to chloroform, which was considered to lower the blood-pressure and depress the heart's action. The cudgels were taken up by Surgeon-Major E. Lawrie, Residency Surgeon to the Nizam of Hyderabad, who, at the Afzulgunj Hospital, had evolved his own method of administration; this was a single dose technique which was used for all minor surgery, the "chloroformists" being students who acted for a month at a time under Lawrie's supervision. In 1888 Lawrie persuaded the Nizam to finance an investigation with the object of overthrowing the Glasgow report and of proving his technique to be entirely safe. The First Hyderabad Commission, working

with small mammals, found in favour of chloroform, but the findings were received with scepticism in Great Britain; in consequence, the *Lancet* proposed a second commission, sending Lauder Brunton out as an independent observer; at the same time, the Editor of the *Lancet*, Thomas Walkley Jun., asked Buxton to make a full investigation into the clinical use and the mortality of chloroform in Great Britain and Europe.

The findings of the Second Commission were unfavourable to chloroform, but Buxton largely disagreed with the validity of the evidence, on the grounds that the experimental work had been performed on pariah dogs and was therefore not applicable to the human subject. His own findings, based on his investigation, were published in the *Lancet* in 1893 and may be summed up as follows:

That ether is the safest anæsthetic for major surgery.

That nitrous oxide should replace chloroform in minor surgery.

That chloroform is never devoid of risk.

That the death rate under chloroform had been unduly high and could be lowered by improved methods and greater care.

That every anæsthetic required the undivided attention of a trained medical man.

In 1901, a third Chloroform Commission was financed by the British Medical Association; it was a distinguished committee, of which Buxton was secretary, numbering among its members his two life-long friends Victor Horsley and Vernon Harcourt. The findings of the commission constituted a personal triumph for Buxton and for the dosimetric method of administration which he advocated, and which he had worked out with the aid of Harcourt and the inhaler which bears the latter's name.

Although, to his contemporaries, Buxton's work on

chloroform was of supreme importance, it is, to us, overshadowed by the revolution which he brought about in the teaching of anæsthetics.

When Buxton was first appointed anæsthetist, teaching was of a casual and rudimentary nature. The majority of anæsthetics were administered by the R.M.O.; two clerks were attached to him, but they were forbidden to speak or to touch the apparatus during the administration; on the theoretical side, Clover occasionally lectured on some important recent advance. From the very day of his appointment, Buxton endeavoured, in the face of fierce opposition, to give a systematic course of teaching. At first, his lectures were mere "stop-gaps" given on Mondays at the invitation of Mr. Christopher Heath, when the latter was unable to lecture; even when Buxton was permitted to give a regular course, it did not form part of the students' compulsory curriculum, and the fact that Buxton's lectures were always well attended testifies to his skill as a teacher. Some years later and after a prolonged struggle, he managed to induce the authorities to give permission for the students to administer anæsthetics under his supervision.

As a teacher, Buxton was a martinet, insisting on attention to detail and using clear-cut and forceful injunctions; his students stood in considerable awe of him, but his enthusiasm, his pains-taking instruction and his sense of humour achieved for him a large measure of popularity. So successful was his undergraduate teaching that it was said that a University College Hospital student could always be recognized in after-life by his ability to give a competent anæsthetic. Nor was he successful with students alone; post-graduates flocked to his demonstrations and he visited Paris and Lausanne by invitation, although it appears that he made little headway against the resistance of continental surgeons to general anæsthesia.

In person, Buxton was the typical Victorian father, tall, bearded and with an imperious eye; for years he was a familiar figure in Wimpole Street, with his grey frock coat and grey topper, carrying his bag containing three cylinders from one dentist's consulting room to another. He read papers and lectured before many learned bodies in spite of the fact that he suffered from a severe speech defect. As a writer he had a superb command of the English language; his essay "Death and her Twin-Sister, Sleep" (published in the *Contemporary Review*) is a beautiful piece of writing, while his text-book, which ran into six editions, is a model of lucid prose. Towards the end of his career, Buxton interested himself in the history of his subject and he wrote a number of papers, including the first account of Crawford Long's experiments to be published in Britain, and a full account of Hickman's work. But, although his knowledge of classical medicine and of pre-anæsthetic attempts to relieve pain was excellent, these are the least satisfactory of Buxton's writings, for he had not the critical mind and was too much given to take his "facts" for granted.

After his retirement, owing to illness, in 1919, Buxton lived at a house which he had built some years previously at Boxmoor in Hertfordshire. Here he devoted his remaining years to gardening and the lore of the countryside; but he may be said to have died in harness, for he continued to teach nurses and administer anæsthetics at the West Herts Hospital almost until the day of his death, which occurred on his seventy-sixth birthday, June 28th, 1931.

Anæsthesia as we know it to-day is the work of many men; of all those who have gone before, Dudley Wilmot Buxton, teacher, thinker and scientist, must rank among the highest.

FROM THE MORBIDITY CONFERENCE

OUT-PATIENT DEATH FOLLOWING THE USE OF THIOPENTONE

MR. A., a man of 57 years and considerably overweight, had been attending the out-patient department for heart failure. He had not thought it necessary to attend during the previous few weeks and was not taking any medicines. He was able to walk about with reasonable ease, but walking up a flight of stairs made him short of breath.

He developed a subcutaneous abscess on the lateral aspect of his left forearm, which was treated conservatively for about a week. It was then decided that, having due regard to his general condition, he would have to have the abscess opened under general anæsthesia.

The Resident Anæsthetist was called, and being informed of the history of the patient, decided that nitrous oxide and oxygen would not be a suitable anæsthetic. In view of the fact that Mr. A. was able to walk to the hospital and walk up stairs to reach the Minor Operations Theatre, the anæsthetist felt that a small dose of thiopentone followed immediately by inhalation of oxygen would be the safest type of anæsthetic. He went to the extent of mixing 1 ml. of "coramine" with 0.4 g. of thiopentone in a 10 ml. syringe. He had previously used this mixture in anæsthetizing patients for appendicectomy and other surgical emergencies and it had cut out almost entirely the transitory respiratory depression which is often associated with the administration of thiopentone.

Mr. A. climbed on to the operating table unaided, and was given 2 ml. of the 10 ml. mixture containing 0.4 g. of

thiopentone, and 1 ml. of coramine. The anæsthetist asked the patient if he was quite comfortable and being reassured on this point, he gave a further 2 ml. of the mixture. After telling the patient that he would shortly begin to feel sleepy and receiving the reply that the patient did not feel at all sleepy, he gave a further 2 ml. of the mixture. After allowing what he thought to be a reasonable length of time to elapse, in order to allow for Mr. A.'s slow circulation, and being told by the patient that he felt he would never go to sleep, the anæsthetist then gave the rest of the contents of the syringe. He withdrew the needle from the vein, put the syringe down, walked to the anæsthetic machine at the patient's head, and immediately applied the mask giving pure oxygen. It was noted that the patient's respiration had failed but no undue alarm was felt. Artificial respiration using pure oxygen was given, there still being no apparent cause for alarm. The patient's chest expanded easily on pressure of the reservoir bag but after a minute of this treatment his colour began to change. Continued artificial respiration with pure oxygen and with an observed clear airway did not improve the patient's colour, which became dark blue. At this stage a gum elastic catheter was passed into the trachea over the first and second fingers of the left hand with comparative ease and was shown to be in the trachea. Oxygen was blown through this catheter but the patient still failed to respond. Artificial respiration was therefore assisted by manual compression of the chest by the surgeon, and a further 2 ml. of coramine was injected into the heart. The patient did not respond to any of this treatment and after 15 minutes was pronounced dead.

At post-mortem examination Mr. A. was found to have a grossly enlarged heart and liver with signs of toxæmia, chronic bronchitis and adhesions of his right lung to the

right chest wall. The heart weighed 29 ozs.; there was moderate hypertrophy of the left ventricle, with gross dilatation of the right auricle. The valves were healthy and the coronary arteries patent and somewhat dilated. The heart muscle was soft, in keeping with the toxæmia. There was moderate atheroma of the aorta. The liver was enlarged $\times 2$, weighing 18 ozs. and showing signs of chronic passive congestion.

Looking back on this incident, it is obvious that Mr. A. received a dose of thiopentone which, in his condition, was too great. Among recently qualified men there is often too little realization of (i) the very slow circulation time in elderly patients—especially those with any form of heart disease, and (ii) the ease with which an overdose of an intravenous drug may be given once the needle is in the vein.

It is debatable whether thiopentone should be given to patients in any form of heart failure, since there is some evidence that, besides affecting the respiratory centre, thiopentone does have a direct effect on the myocardium. This with peripheral vasodilation causes a transitory lowering of diastolic blood-pressure which may be sufficient to cause fatal myocardial anoxia in such patients.

ON HANDING OVER THE PATIENT

A patient was being anæsthetized for an obstructive lesion of the right middle lobe. There was a considerable production of sputum and blood during the difficult dissection of the lobe and constant suction was required. The cuff of the endotracheal tube burst. In view of the leakage of gases which resulted it was decided to insert a pharyngeal pack in order to see if it were possible to avoid changing the tube. This was done and an airtight circuit resulted.

At the end of the operation, after the administration of antidote drugs, the anæsthetist handed the patient over to the Registrar to remove the endotracheal tube, but did not mention the pharyngeal pack. The tube was removed and the patient returned to the ward and visited on two or three occasions during the subsequent hours by the anæsthetist and the surgeon. Although the patient was fully conscious before leaving the operating theatre, during these hours there was no evidence of discomfort or complaint until about three o'clock in the afternoon, the operation having been completed at approximately eleven in the morning, the patient complained that she thought she had something in her throat. The nurse investigated and removed the pharyngeal pack!

The fact that pethidine had been administered may have contributed to the apparent insensitivity of the patient to the presence of the pack.

Brit. J. Anæsth. (1953), **25**, 78.

A PRE-AMPLIFIER WHICH ENABLES ELECTRO-ENCEPHALOGRAMS TO BE RECORDED WITH MOST ELECTROCARDIOGRAPHS

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IN experimental medicine it is sometimes useful to be able to record a single-channel electroencephalogram. Anæsthetists, in particular, are now interested in the effect of anæsthetics upon the encephalogram and may have access to a direct-writing electrocardiograph but not to an electroencephalograph. The unit described can be added to most electrocardiographs, so that they then become suitable for single-channel electroencephalogram recording.

If the performance of the usual electrocardiograph be compared with the requirements of an electroencephalograph, it is possible to specify the performance of the additional pre-amplifier, as follows:

1. Gain—not less than 20 times.
2. In-phase/out-phase rejection ratio—at least 10,000 : 1.
3. "Noise"—less than 2μ volt peak, referred to input.
4. Time constant—2 seconds.

The most difficult requirement is No. 3—"noise". It is necessary to choose a suitable valve type and then to operate it in a suitable circuit at optimal voltages. The new Mullard low-noise pentode, Type EF.40, has proved suitable without special selection of individual valves. We found that if the anode voltage be increased above our figure, "noise" increases, while if the anode voltage be lower, the signal to noise ratio does not further improve,

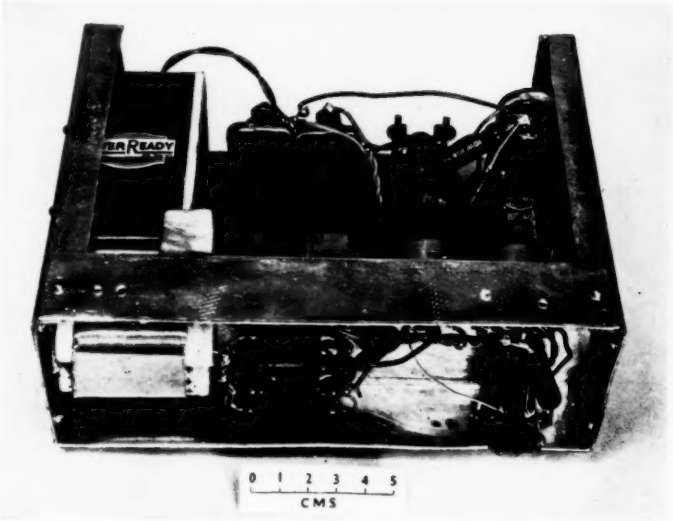

FIG. 1

and gain decreases. The figure chosen is best, and gives, in this circuit, a gain of about 30 times. Lowering the heater voltages from 6 (normal operating voltage) to 4, again diminished "noise"; but below 3 volts on the heaters, the valves do not amplify satisfactorily.

"Noise" was not significantly improved by connecting the valves as triodes; so the advantages, in balance and gain, of pentode connection were retained.

Figure 2 is a tracing produced by applying a 5μ volt "square-wave" to the input of the pre-amplifier and recording from the electrocardiograph to which it was

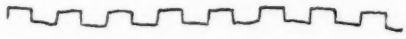

FIG. 2

5μV. Signal applied to pre-amplifier. "Noise" is about 1.25μV. operating conditions.

connected. The equipment was, of course, operating at extreme sensitivity; such sensitivity is rarely needed in practice. The "noise" is about 1.25μ volts with a band width of 50 c.p.s.

Power supplies Table I shows the voltages and currents needed for operation. The high tension currents are so small that even a miniature high tension battery will have a very long life. A low tension accumulator is preferred. A $4\frac{1}{2}$ volt dry battery may be used; but we have found that with some low tension dry batteries a certain amount of low-frequency drift occurs.

Construction and Components We have made the pre-amplifier as a self-contained unit, including batteries, which measures $7\frac{3}{4}'' \times 7\frac{3}{4}'' \times 3''$ (fig. 1). There is little that is critical about component arrangement, however, and individual needs can be met.

TABLE I

Anode Current 38μA
G.2. Current 7.5μA
Cathode Current 91μA. Both Valves
Drain due to resistor chain 400μA
Total H.T. consumption 491μA
L.T. consumption 0.30 amps at 4 volts

Anode Voltage	22	measured from Cathode
G.2. Voltage	15	measured from Cathode
Bias Voltage	0.15	measured from grid to Cathode

The anode and grid resistors should be of the high stability type. The two 16μ F condensers C.2 and C.3 should be of high quality with a leakage current less than 4μ A at 15 volts (fig. 3).

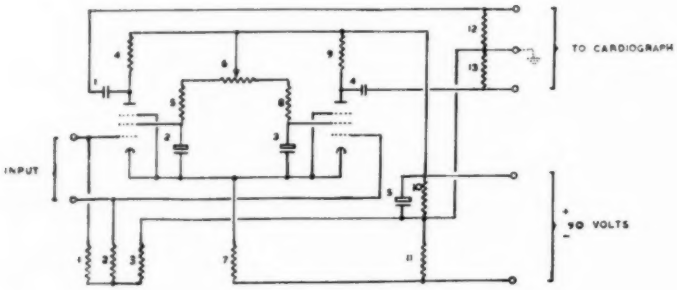

FIG. 3
Circuit Diagram.

R.	1	0.5 meg.	6	1 meg.	11	150 K.	C.	1	2μF.
	2	0.5 meg.	7	660 K.	12	10 meg.		2	16μF.
	3	1 meg.	8	1.5 meg.	13	10 meg.		3	16μF.
	4	220 K.	9	220 K.				4	2μF.
	5	1.5 meg.	10	75 K.				5	150μF.

The 2μ F (C_1 & C_4) coupling condensers must have very high leakage resistances.

The authors believe that with the valves chosen the circuit and components give optimum results, and we have found that even minor deviations lead to disappointing results.

Figure 4 shows sample electroencephalograms under anæsthesia obtained with this pre-amplifier and a conventional direct-writing electrocardiograph.

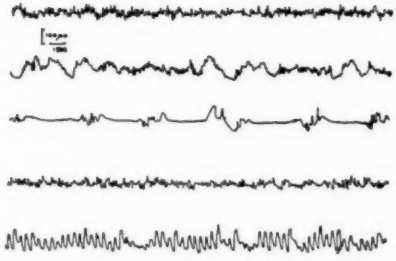

FIG. 4

Encephalogram Tracings obtained with the equipment.

Line 1—Light Thiopentone Anæsthesia
„ 2—Moderate „ „
„ 3—Deep „ „
„ 4—Light Ether Anæsthesia
„ 5—Moderate „

CORRESPONDENCE

A NOTE ON THE MODE OF ACTION OF NEUROMUSCULAR BLOCKING SUBSTANCES

Sir,

It has been suggested by Zaimis (Zaimis, 1952) that decamethonium produces a neuromuscular block initially by depolarization and subsequently by a process of competitive inhibition. In support of this suggestion may be advanced the clinical observation that in certain circumstances neostigmine is effective as an antidote to the neuromuscular block produced by decamethonium.

Tensilon (3 hydroxy-phenyl dimethylethyl ammonium bromide), an anti-curare compound having very little anticholinesterase activity, is found to be almost as effective as neostigmine.

We have observed that the gasping respiration and paresis occurring after large or repeated doses of decamethonium, described by Gray, Hunter, and Harris and Dripps (Gray, 1950; Hunter, 1950; Harris and Dripps, 1950), is rapidly restored to normal by neostigmine or Tensilon.

No reversal by neostigmine or Tensilon is found when complete paralysis by decamethonium is present.

The paretic condition, which is only seen after large or repeated doses of decamethonium and after the initial depolarizing block has worn off, differs from that produced by curare in that it may persist for at least six hours unless terminated by neostigmine.

Recently some evidence has been presented suggesting that large doses of relaxants can produce respiratory de-

pression by a central action (Ellis, Morgan, and de Beer, 1952). The characteristic paresis following large doses of decamethonium is not affected by nikethamide, a central respiratory stimulant.

The mutual antagonism of the two modes of action of decamethonium may afford an explanation of the tachyphylaxis seen with decamethonium (Scurr, 1951). Antagonism between curare and decamethonium (depolarizing action) has already been demonstrated (Paton and Zaimis, 1948; Paton and Zaimis, 1949) and also between gallamine and decamethonium (Hunter, 1952).

In man appearances suggestive of block by competitive inhibition with succinylcholine have not yet been seen with doses of up to 1,000 mg. of iodide.

The myasthenic neuromuscular junction is hypersensitive to block by competitive inhibition and insensitive to block by depolarization.

If, therefore, the suggestion of the dual action of decamethonium is correct and that its second or competitive inhibitive mode of action can be demonstrated in man by the use of large doses, it would be expected that the myasthenic would be resistant to small doses of decamethonium which produce depolarization only, and very sensitive to large doses which produce competitive inhibition. The observations of Churchill-Davidson and Richardson (Churchill-Davidson and Richardson, 1952a; Churchill-Davidson and Richardson, 1952b) confirm that this is the case.

Presumably the depolarization caused by decamethonium at the normal neuromuscular junction masks any competitive inhibitory process, except where large doses are employed. At the myasthenic neuromuscular junction, however, is found not only a partial block by competitive inhibition, but also a (possibly complementary)

resistance to depolarization. Consequently conditions favour the demonstration of the competitive inhibitory action of decamethonium at a much lower dosage than that at which it can be seen at the normal neuromuscular junction, a dosage which is, however, considerably above that required to cause block by depolarization in the normal subject.

The apparently anomalous observation by Churchill-Davidson and Richardson that resistance to decamethonium is most marked in those myasthenics having only mild symptoms may now be explained on the assumption that in addition to the high resistance to depolarization only slight block due to competitive inhibition is present, as evidenced by the mildness of the symptoms. Consequently a large dose of decamethonium is required to produce appreciable block by competitive inhibition.

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REFERENCES

Churchill-Davidson, H. C., and Richardson, A. T. (1952a). *Proc. R. Soc. Med.*, **45**, 179.
— — (1952b.) *J. Neurol. Psychiat.*, **15**, 129.
Ellis, C. H., Morgan, W.V., and de Beer, E. J. (1952). *J. Pharmacol.*, **106**, 353.
Gray, A. J. (1950). *Lancet*, **1**, 253.
Harris, C., and Dripps, R. D. (1950). *Anesthesiology*, **11**, 215.
Hunter, A. R. (1950). *Brit. J. Anæsth.*, **22**, 218.
— — (1952). *Proc. R. Soc. Med.*, **45**, 186.
Paton, W. D., and Zaimis, E. J. (1948). *Nature, Lond.*, **161**, 718.
— — (1949). *Brit. J. Pharmacol.*, **4**, 381.
Scurr, C. F. (1951). *Brit. J. Anæsth.* **23**, 103.
Zaimis, E. J. (1952). *Nature, Lond.*, **170**, 617.

REVIEWS

Essentials of General Anæsthesia. By R. R. MACINTOSH and F. B. BANNISTER, 5th Edn. Published by Blackwell Scientific Publications. 40*s*.

THIS book has been modernized by the addition of a chapter on the muscle relaxants.

Apart from that, very few changes have been made since the last edition which appeared in 1947.

Principles and Practice of Anesthesiology. By VINCENT J. COLLINS. Published by Henry Kimpton, London. Pp. 528, 99 illustrations. 75*s*.

THE author of this work was faced during World War II with the task of instructing anæsthetists, and for this purpose felt there was a need for a single volume which would contain all the information required by the anæsthetist in the early stages of his training.

The book which he has produced to fill this gap is of some 500 pages, and includes, besides several chapters on the relevant physiology, sections dealing with regional techniques, pharmacological considerations, complications, anæsthesia for special surgical problems, and also with intravenous and inhalation therapy. The author states that "such a monumental task undertaken by one person could not possibly be exhaustive." This is undoubtedly so, and therefore one feels that in the absence of the special circumstances which resulted in the conception of the work, there is perhaps little call for a volume of this nature which is too comprehensive for the newcomer to the specialty to help him through his first days in the theatre, and is in

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— — (1952). *Proc. R. Soc. Med.*, **45**, 186.
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— — (1949). *Brit. J. Pharmacol.*, **4**, 381.
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many of its sections too scanty to be of value to the trainee seeking the detailed knowledge of the basic sciences which is demanded of present day entrants to the specialty. In fact the book appears to fall between two stools, being neither an elementary book, nor yet of great value to the serious student of the subject.

The feature of the book which commends itself to the reader is the really extensive bibliography, which should prove of great value. The references given are largely from American sources, and there are some noteworthy omissions of British publications.

As in all larger text-books the descriptions of the newer techniques and drugs which, nevertheless, have in a short time become a part of everyday anæsthetic practices are brief. An example of this is the section on the relaxant drugs, which occupies only eight pages. In this section the rather astonishing statement is made that it is difficult to see why the curare-like substances should be antagonized by physostigmine or neostigmine and that as yet there is no proof that they are effective antagonists.

One need hardly say that the classical aspects of anæsthesia, that is to say, the descriptions of the signs and stages, the pharmacology of the inhalation agents, etc., are all adequately covered.

In summary, a useful book, mainly for its extensive bibliography.

FACULTY OF ANÆSTHETISTS

ROYAL AUSTRALASIAN COLLEGE OF SURGEONS

A FACULTY of Anæsthetists within the Royal Australasian College of Surgeons was formally inaugurated on 25th August, 1952, at the College.

At that meeting Sir Gordon Gordon-Taylor presented to the Faculty an illuminated message from the Faculty of Anæsthetists of the Royal College of Surgeons of England.

The object of the Faculty is to improve, by all means possible, the art and science of Anæsthetics. In this object the College is most anxious to help.

As soon as an election can be held in accordance with the regulations approved on the 25th August, 1952, a Board of the Faculty, which shall govern its affairs, will be elected. In the meantime an Acting Board, consisting of Sir Victor Hurley, Mr. Henry Searby, Drs. H. J. Daly, J. Ellis Gillespie, S. V. Marshall, D. G. Renton, L. G. Travers and G. R. Troup, was authorized to act under the Chairmanship of the Acting Dean, Dr. D. G. Renton.

The establishment of this Faculty is the happy culmination of the efforts of Sir Victor Hurley and Mr. Henry Searby; together with Drs. H. J. Daly, G. R. Troup, D. G. Renton, L. G. Travers and J. Ellis Gillespie, who were appointed by the Australian Society of Anæsthetists in 1950 to conduct the necessary negotiations with the College. With the general approval of the Australian Society of Anæsthetists, forty Foundation Fellows and sixty-two Foundation Members were invited to join. In future, in accordance with the regulations, applications for membership will be received from anæsthetists with

appropriate qualifications, and recommendations will be made to the College Council for admission to membership of those approved by the Board of the Faculty. The Board may also submit a limited number of names annually to the College Council for election to Fellowship of the Faculty.

The Secretary of the Faculty is Mr. H. G. Wheeler, Royal Australasian College of Surgeons, Spring Street, Melbourne, C.1, to whom all enquiries should be addressed.

The Australian Society of Anæsthetists is to be congratulated on its wish to establish this scientific body which it believed was a natural development of that Association; the functions of the Faculty will be essentially educational and academic, and will not in any way lessen the importance of, or the work done by the Australian Society of Anæsthetists.

[Photo by Harold Moyse

A. CHARLES KING